

Eppur si muove...

La terapia nel MONDO LINFOMI

***Linfoma diffuso a grandi
cellule B: ottimizzazione
diagnostica***

Stefano A. Pileri



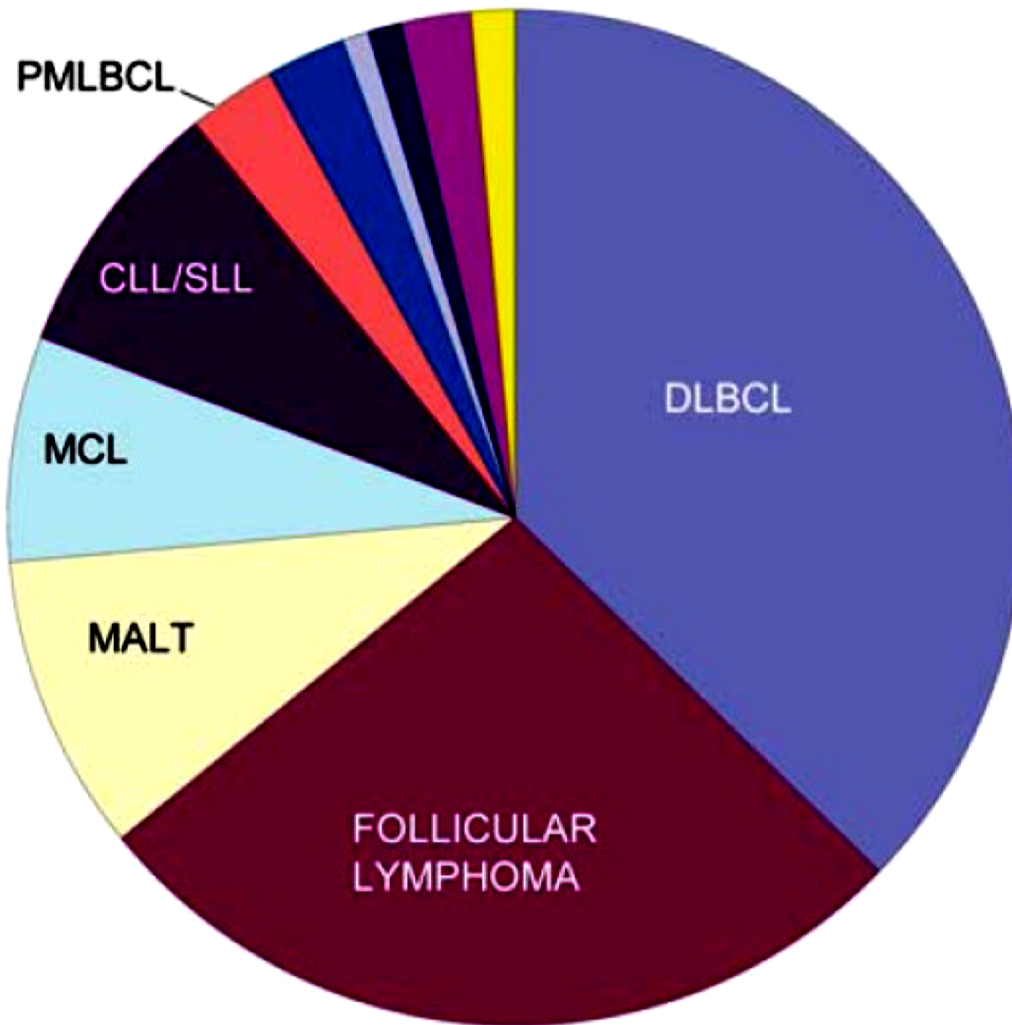
Istituto
Europeo
di Oncologia



VERONA, 2 MAGGIO 2022

Disclosures of Stefano A. Pileri

Company name	Research support	Employee	Consultant	Stockholder	Speakers bureau	Advisory board	Other
BeiGene						X	
Takeda						X	
Roche					X		
Diatech						X	



■ Diffuse large B-cell 37%

■ Follicular 29%

■ MALT lymphoma 9%

■ Mantle cell lymphoma 7%

■ CLL/SLL 12%

■ Primary med large B-cell 3%

■ High Grade B, NOS 2.5%

■ Burkitt 0.8%

■ Splenic marginal zone 0.9%

■ Nodal marginal zone 2%

■ Lymphoplasmacytic 1.4%

Diffuse large B-cell lymphoma: variants, subgroups and subtypes/entities

Diffuse large B-cell lymphoma, noth otherwise specified (NOS)

Common morphologic variants

Centroblastic

Immunoblastic

Anaplastic

Other rare variants

Molecular subgroups

Germinal centre B-cell-like (GCB)

Activated B-cell-like (ABC)

Diffuse large B-cell lymphoma subtypes

T-cell/histiocyte-rich large B-cell lymphoma

Primary DLBCL of the CNS

Primary cutaneous DLBCL, leg type

EBV-positive DLBCL, NOS

*Large B-cell lymphoma with IRF4 rearrangements**

Other lymphomas of large B-cells

Primary mediastinal (thymic) large B-cell lymphoma

Intravascular large B-cell lymphoma

DLBCL associated with chronic inflammation

Lymphomatoid granulomatosis

ALK-positive large B-cell lymphoma

Plasmablastic lymphoma

HHV-8-positive DLBCL, NOS

Primary effusion lymphoma

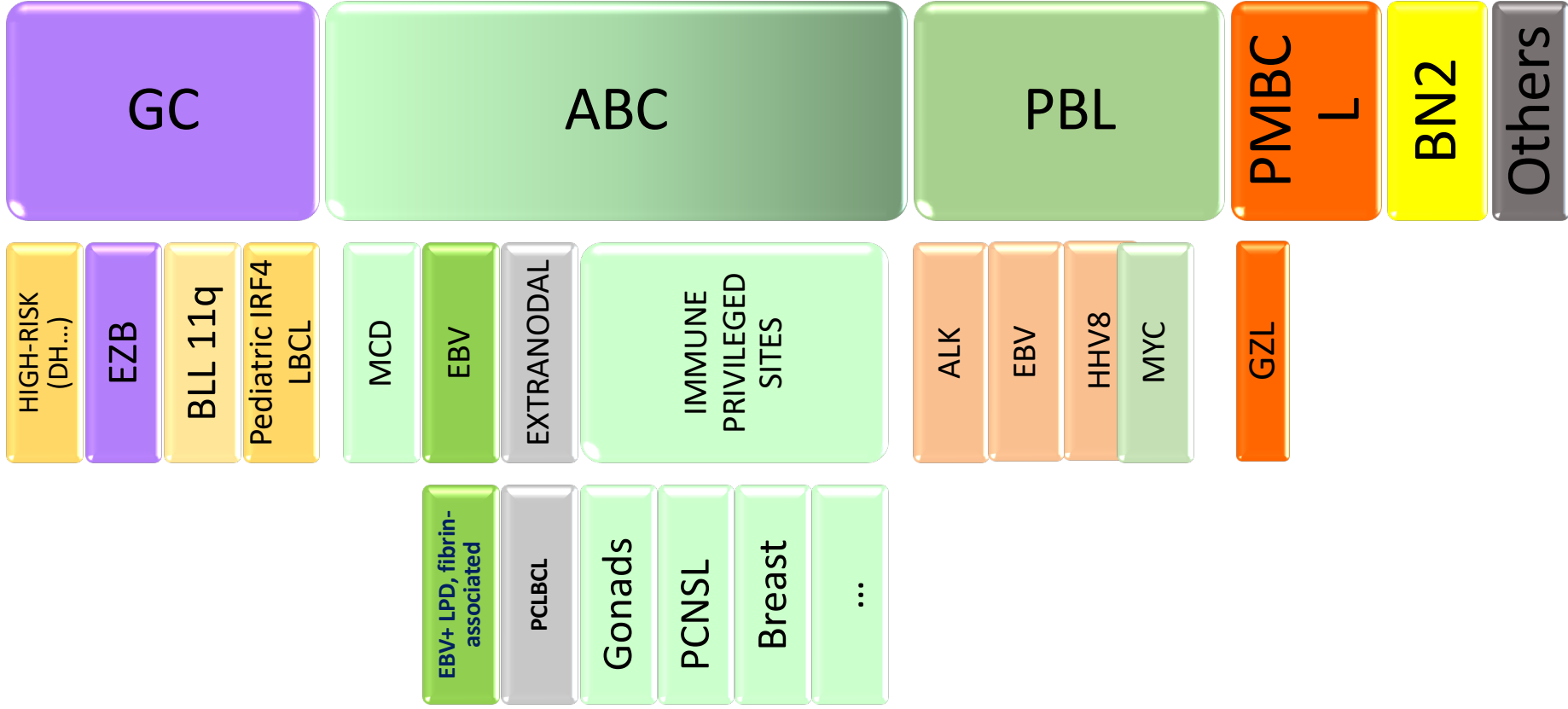
New provisional categories

High grade B-cell lymphoma

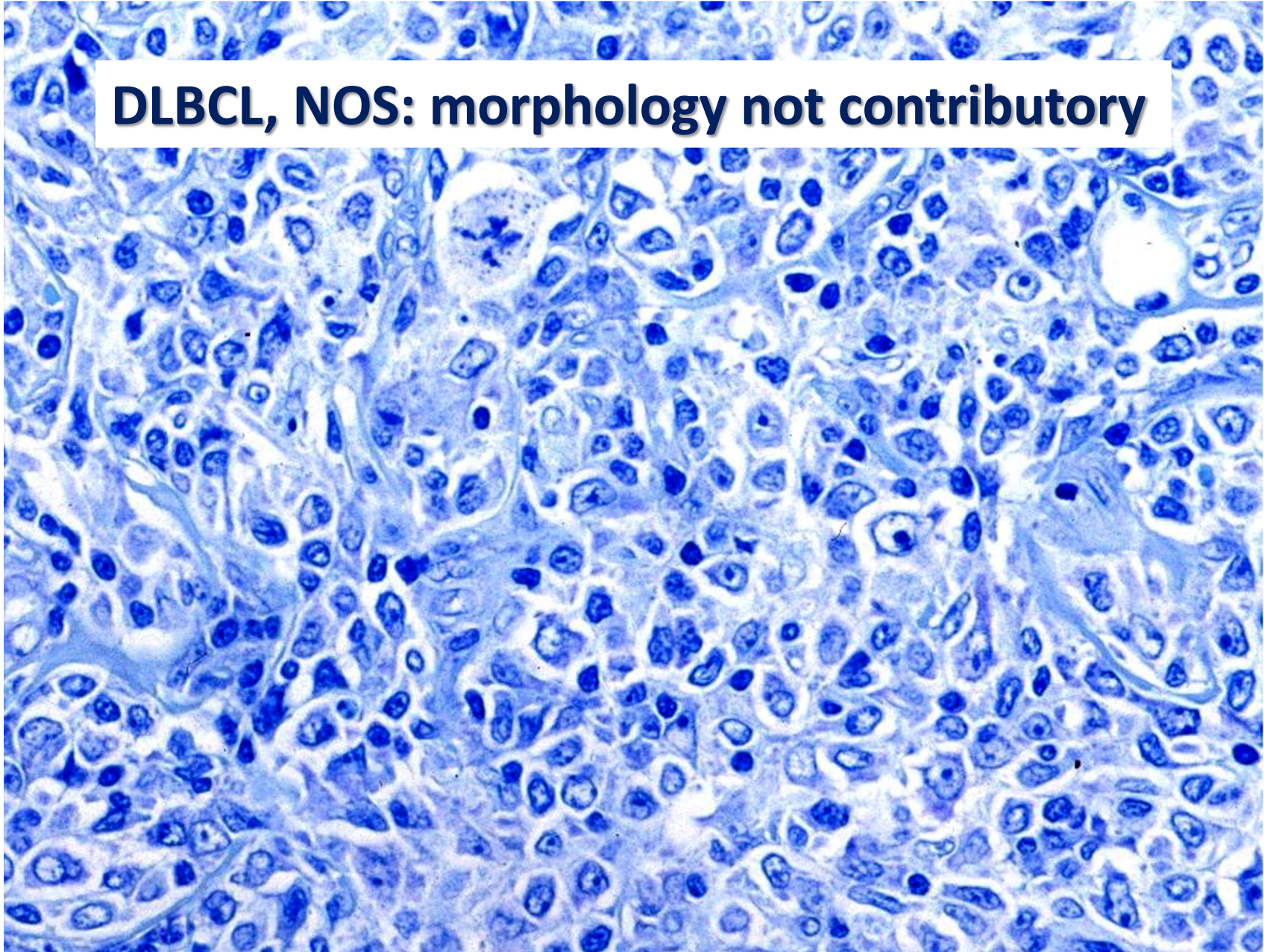
High grade B-cell lymphoma, with *BCL2* and/or *BCL6* and *MYC* rearrangements

High grade B-cell lymphoma, NOS

Large B-Cell Lymphoma



DLBCL, NOS: morphology not contributory

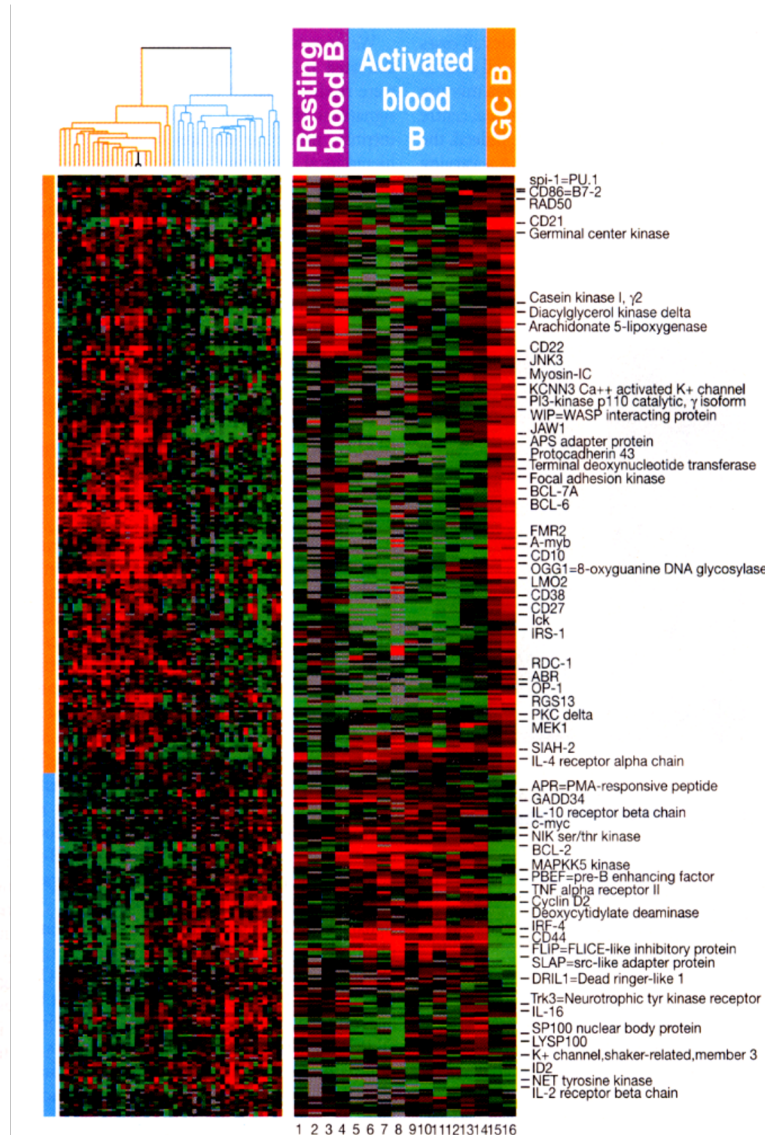
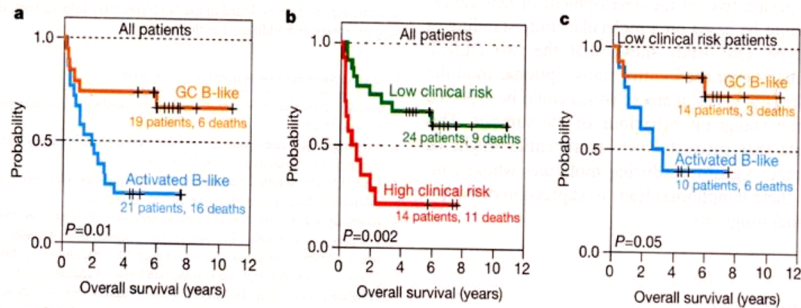


Front-MIND

Distinct types of diffuse large B-cell lymphoma identified by **gene expression profiling**

Alizadeh AA et al.

Nature 2000, 403: 503-11



Original limitation:

**need for fresh or frozen tissue, available
in only a few patients!**

Ideally, tool to apply to FFPE samples!

Gene-expression profiling and not immunophenotypic algorithms predicts prognosis in patients with diffuse large B-cell lymphoma treated with immunochemotherapy

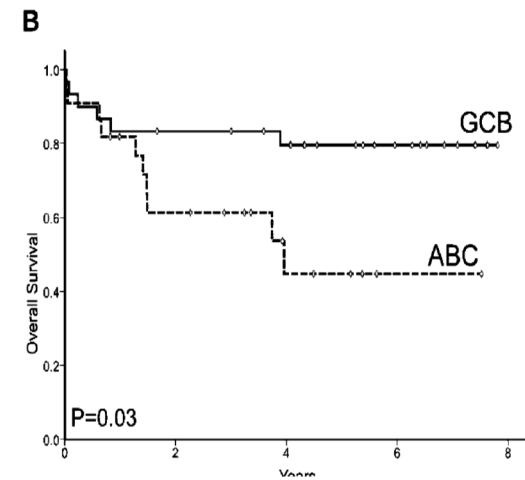
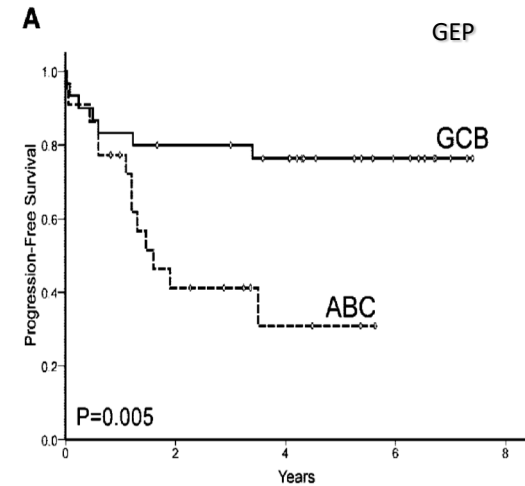
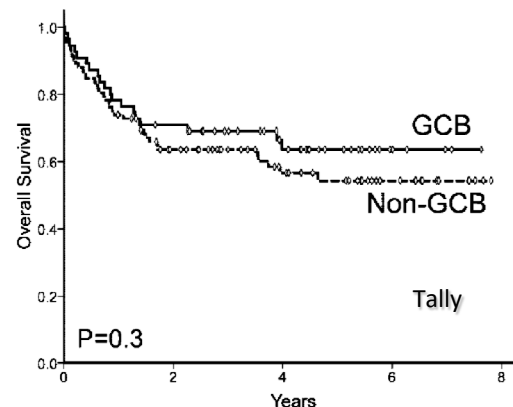
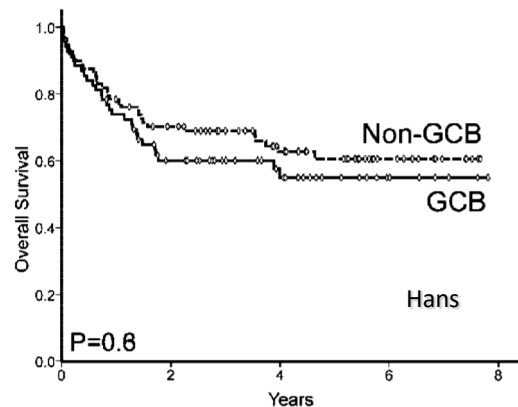
*Gonzalo Gutiérrez-García,¹ *Teresa Cardesa-Salzman,¹ Fina Climent,² Eva González-Barca,² Santiago Mercadal,² José L. Mate,³ Juan M. Sancho,³ Leonor Arenillas,⁴ Sergi Serrano,⁴ Lourdes Escoda,⁵ Salomé Martínez,⁵ Alexandra Valera,¹ Antonio Martínez,¹ Pedro Jares,¹ Magdalena Pinyol,¹ Adriana García-Herrera,¹ Alejandra Martínez-Trillos,¹ Eva Giné,¹ Neus Villamor,¹ Elías Campo,¹ Luis Colomo,¹ and Armando López-Guillermo,¹ for the Grup per l'Estudi dels Limfomes de Catalunya i Balears (GELCAB)

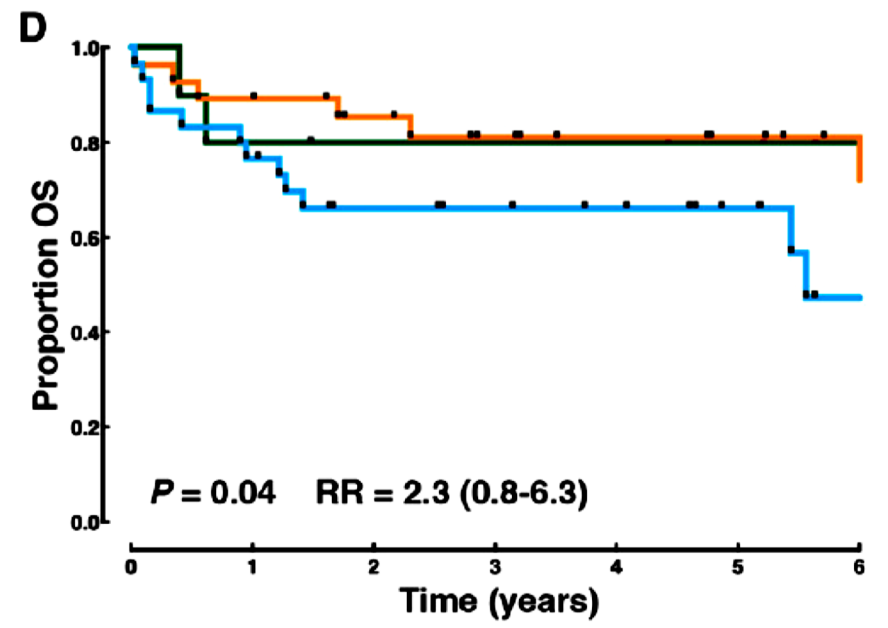
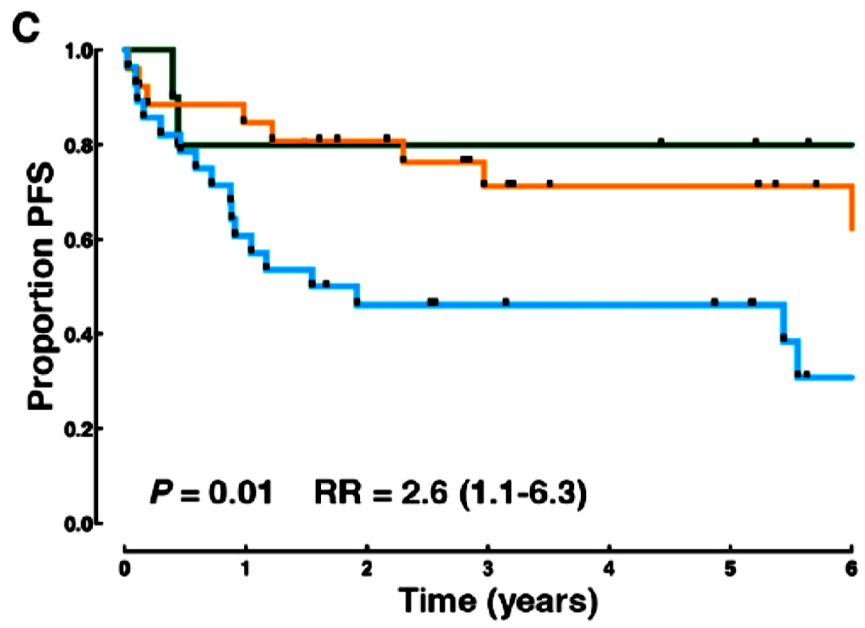
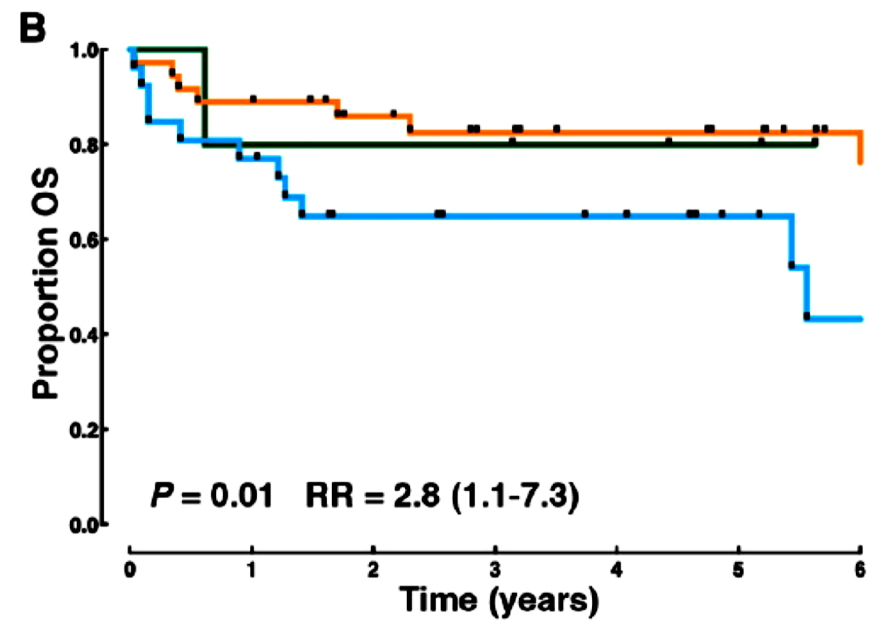
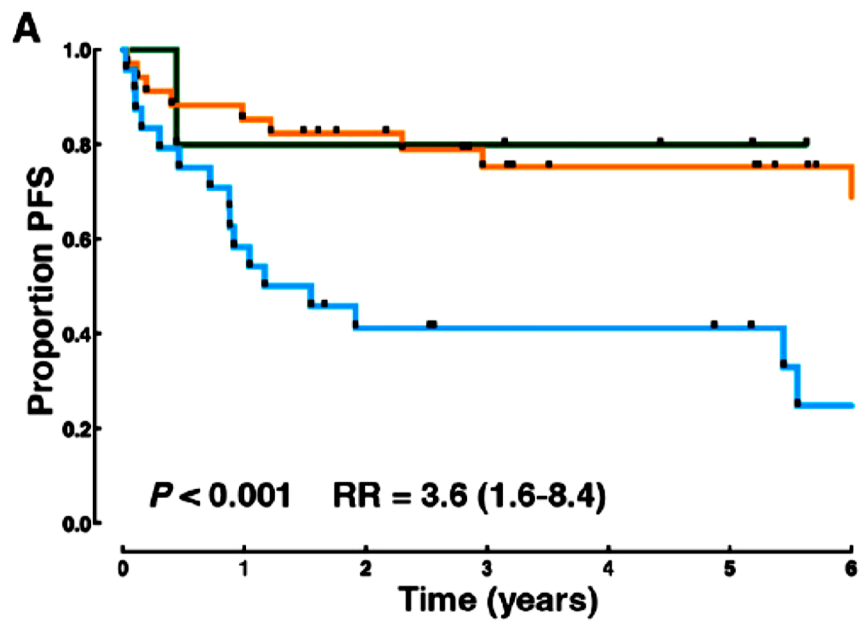
¹Departments of Hematology and Pathology, Hospital Clínic, University of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain; ²Hospital Duran i Reynals, Hospitalet de Llobregat, Spain; ³Hospital Germans Trias i Pujol, Badalona, Spain; ⁴Hospital del Mar, Barcelona, Spain; and ⁵Hospital Joan XXIII, Tarragona, Spain

Diffuse large B-cell lymphomas (DLBCLs) can be divided into germinal-center B cell-like (GCB) and activated-B cell-like (ABC) subtypes by gene-expression profiling (GEP), with the latter showing a poorer outcome. Although this classification can be mimicked by different immunostaining algorithms, their reliability is the object of controversy. We constructed tissue microarrays with samples of 157 DLBCL patients homogeneously treated with immunochemotherapy to apply the following algorithms:

Colomo (MUM1/IRF4, CD10, and BCL6 antigens), Hans (CD10, BCL6, and MUM1/IRF4), Muris (CD10 and MUM1/IRF4 plus BCL2), Choi (GCET1, MUM1/IRF4, CD10, FOXP1, and BCL6), and Tally (CD10, GCET1, MUM1/IRF4, FOXP1, and LMO2). GEP information was available in 62 cases. The proportion of misclassified cases by immunohistochemistry compared with GEP was higher when defining the GCB subset: 41%, 48%, 30%, 60%, and 40% for Colomo, Hans, Muris, Choi,

and Tally, respectively. Whereas the GEP groups showed significantly different 5-year progression-free survival (76% vs 31% for GCB and activated DLBCL) and overall survival (80% vs 45%), none of the immunostaining algorithms was able to retain the prognostic impact of the groups (GCB vs non-GCB). In conclusion, stratification based on immunostaining algorithms should be used with caution in guiding therapy, even in clinical trials. (*Blood*. 2011;117(18):4836-4843)





■ Germinal-Center B-cell-like DLBCL
 ■ Unclassified DLBCL
 ■ Activated B-cell-like DLBCL



Targeted Digital Gene Expression Profiling

RefSeq NCBI	Gene	Length NCBI	Protein aa
NM_002467.4	MYC	2379	454
NM_000633.2	BCL2	6492	239
NM_012452.2	TNFRSF13B	1377	293
NM_014240.2	LIMD1	6284	676
NM_001195286.1	IRF4	5329	451*
NM_194071.3	CREB3L2	7471	520*
NM_006875.3	PIM2	2234	311
NM_001302826.1	CYB5R	1713	276
NM_003929.2	RAB7L1	3324	203
NM_174908.3	CCDC50	8421	306
NM_015361.3	R3HDM1	4722	1099
NM_017706.4	WDR55	2580	383
NM_020701.3	ISY1	3778	285
NM_014607.3	UBXN4	4018	508
NM_030961.2	TRIM56	4723	755
NM_000902.3	MME	5643	750
NM_001284275.1	SERPINA9	1661	435*
NM_024701.3	ASB13	2736	278
NM_018717.4	MAML3	7086	1138
NM_002221.3	ITPKB	6162	946
NM_001080416.3	MYBL1	5192	752
NM_004230.3	S1PR2	3589	353
NM_020529.2	NFKBIA	1579	371
NM_139276.2	STAT3	4978	770
NM_000314.6	PTEN	8718	403*
NM_006218.2	PKI3CA	3724	1068

**26-gene-panel for
COO & key-genes
Haematologica, 2020**

**50-gene-panel for
microenvironment
Ann Oncol, 2018**

MF-
related
genes

DC-
related
genes

CD4⁺ T
cell-
related
genes

<i>ACTA2</i>	Actin, alpha 2, smooth muscle
<i>AEBP1</i>	AE binding protein 1
<i>BGN</i>	Biglycan
<i>COL1A1</i>	Collagen type I alpha 1
<i>COL1A2</i>	Collagen type I alpha 2
<i>COL3A1</i>	Collagen type III alpha 1
<i>COL4A1</i>	Collagen type IV alpha 1
<i>COL5A2</i>	Collagen type V alpha 2
<i>COL6A3</i>	Collagen type VI alpha 3
<i>CTHRC1</i>	Collagen triple helix repeat containing 1
<i>CTSK</i>	Cathepsin K
<i>EGR1</i>	Early growth response 1
<i>FN1</i>	Fibronectin 1
<i>FSTL1</i>	Follistatin like 1
<i>GPNMB</i>	Glycoprotein nmb
<i>LAMB1</i>	Laminin subunit beta 1
<i>LUM</i>	Lumican
<i>MFAP2</i>	Microfibrillar associated protein 2
<i>MMP2</i>	Matrix metalloproteinase 2
<i>MRC2</i>	Mannose receptor, C type 2
<i>MXRAS</i>	Matrix-Remodelling Associated 5
<i>PCOLCE</i>	Procollagen C-endopeptidase enhancer
<i>PLOD2</i>	Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2
<i>POSTN</i>	Periostin, osteoblast specific factor
<i>SPARC</i>	Secreted protein acidic and cysteine rich
<i>SULF1</i>	Sulfatase 1
<i>TGFB1</i>	Transforming growth factor beta induced
<i>ALCAM</i>	Activated leukocyte cell adhesion molecule
<i>AMICA1</i>	Adhesion molecule, interacts with CXADR antigen 1
<i>CD300LF</i>	CD300 molecule-like family member F
<i>COL4A2</i>	Collagen, type IV, alpha 2
<i>IGSF6</i>	Immunoglobulin superfamily, member 6
<i>MDFI1</i>	MyoD Family Inhibitor Domain Containing
<i>P2RY14</i>	Purinergic receptor P2Y, G-protein coupled, 14
<i>SLC29A3</i>	Solute carrier family 29 (nucleoside transporters), member 3;
<i>SLC2A3</i>	Solute carrier family 2 (facilitated glucose transporter),
<i>CTSZ</i>	Cathepsin Z
<i>HS3ST3A1</i>	Heparan Sulfate-Glucosamine 3-Sulfotransferase 3A1
<i>PMP1CB</i>	Peptidase, Mitochondrial Processing Beta Subunit
<i>RAB27A</i>	RAB27A, Member RAS Oncogene Family
<i>SMAD1</i>	SMAD Family Member 1

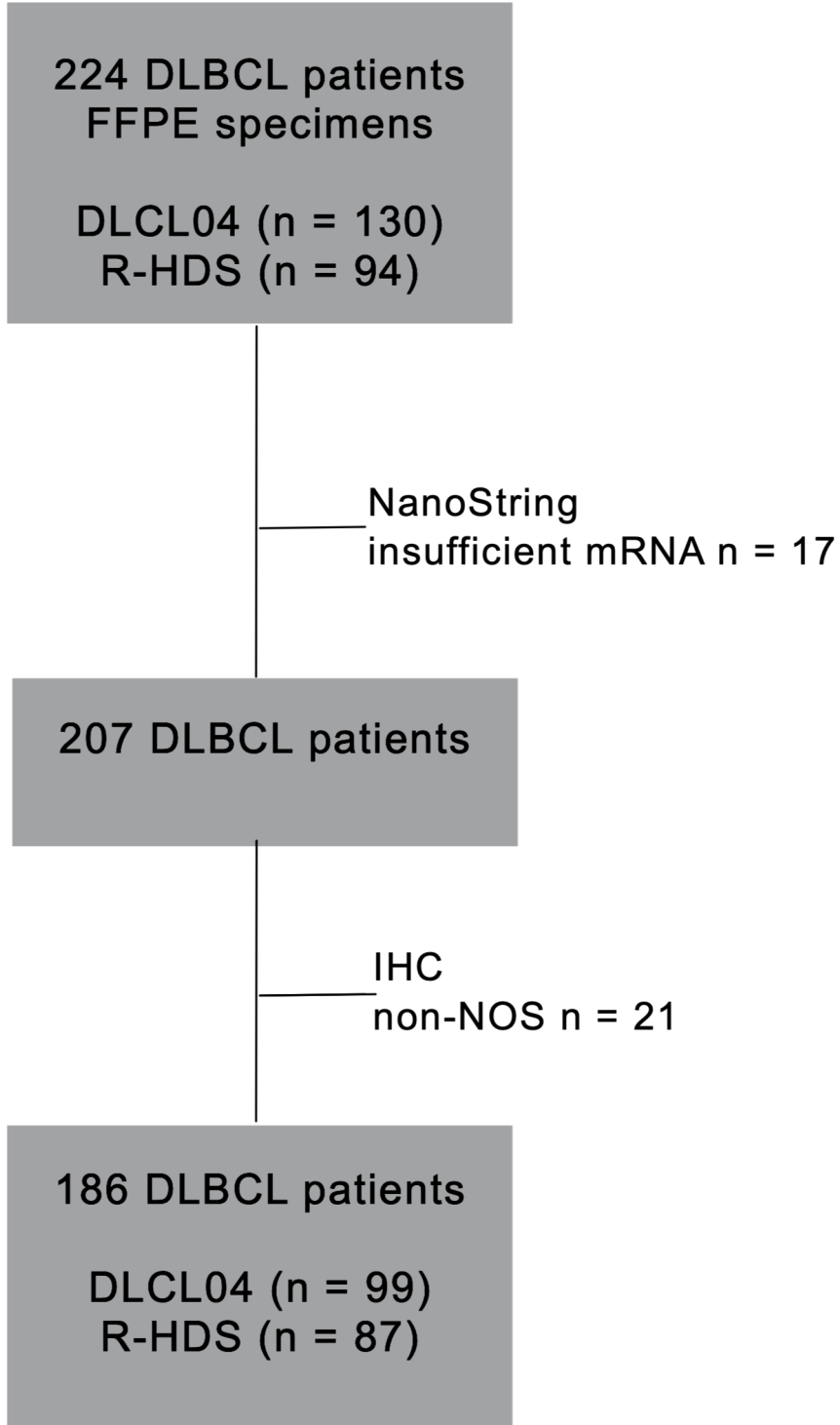
STROMAL
GENES

IMMUNE
GENES

A 3-gene signature based on MYC, BCL-2 and NFKBIA improves risk stratification in diffuse large B-cell lymphoma

by Enrico Derenzini, Saveria Mazzara, Federica Melle, Giovanna Motta, Marco Fabbri, Riccardo Bruna, Claudio Agostinelli, Alessandra Cesano, Chiara Antonia Corsini, Ning Chen, Simona Righi, Elena Sabattini, Annalisa Chiappella, Angelica Calleri, Stefano Fiori, Valentina Tabanelli, Antonello Cabras, Giancarlo Pruneri, Umberto Vitolo, Alessandro Massimo Gianni, Alessandro Rambaldi, Paolo Corradini, Pier Luigi Zinzani, Corrado Tarella, and Stefano Pileri

Haematologica 2020 [Epub ahead of print]

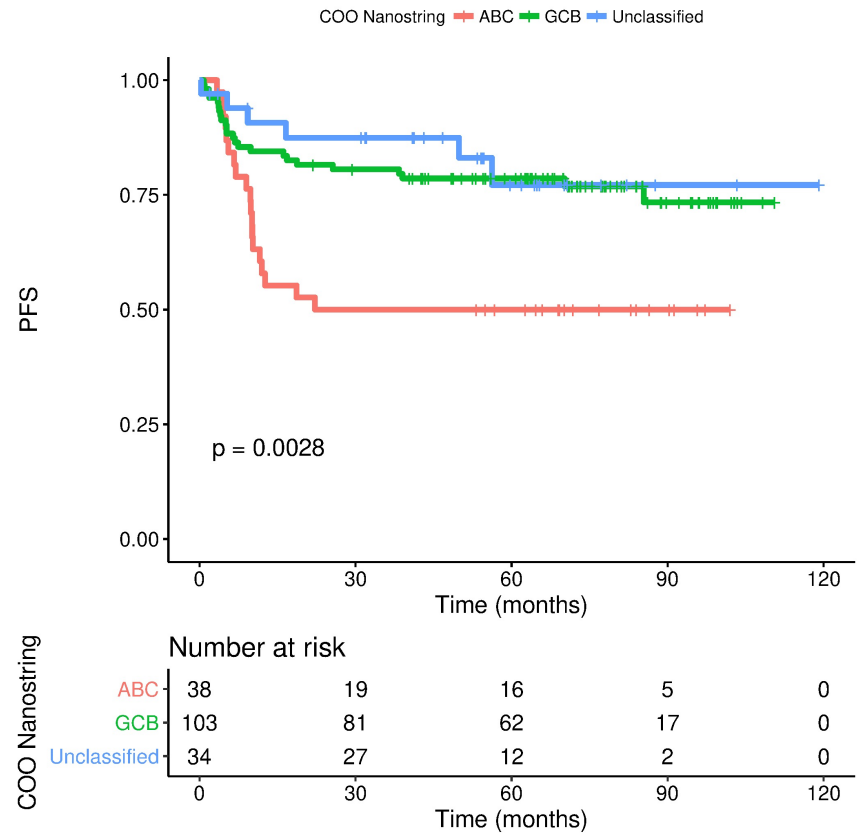
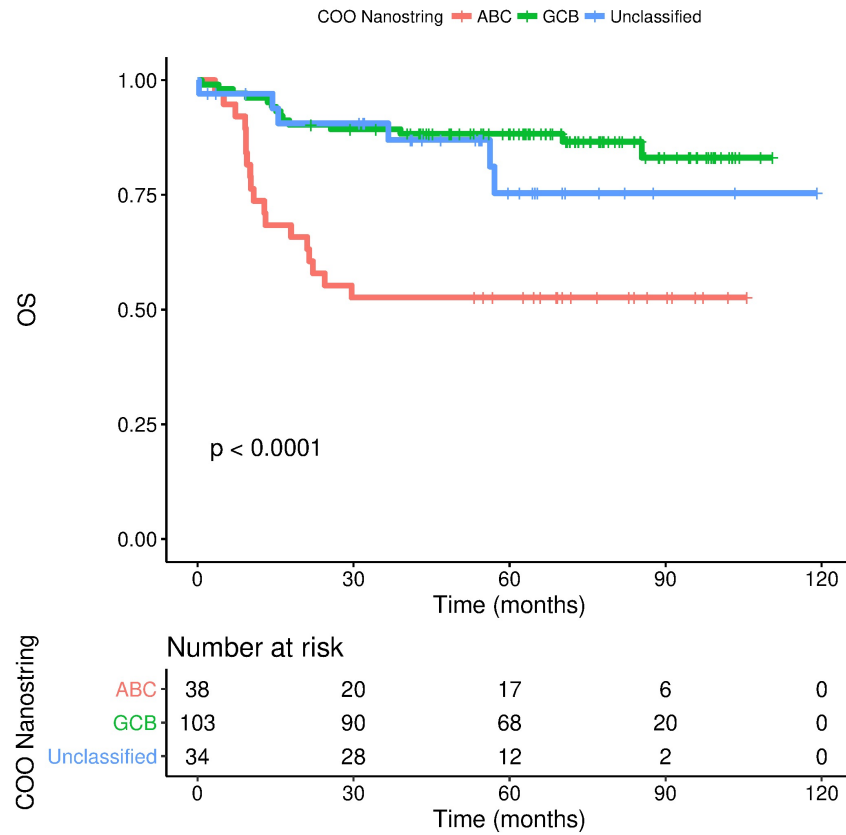


In both trials, only patients staged III-IV were enrolled, all treated with R-CHOP or R-CHOP-like therapies followed or not by Auto-SCT.

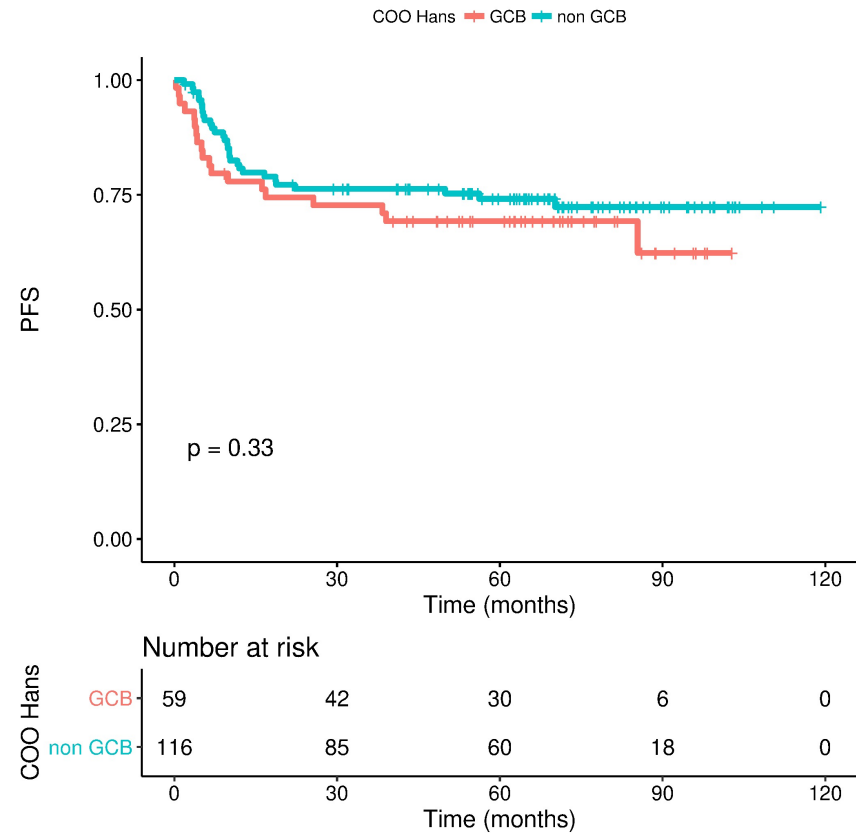
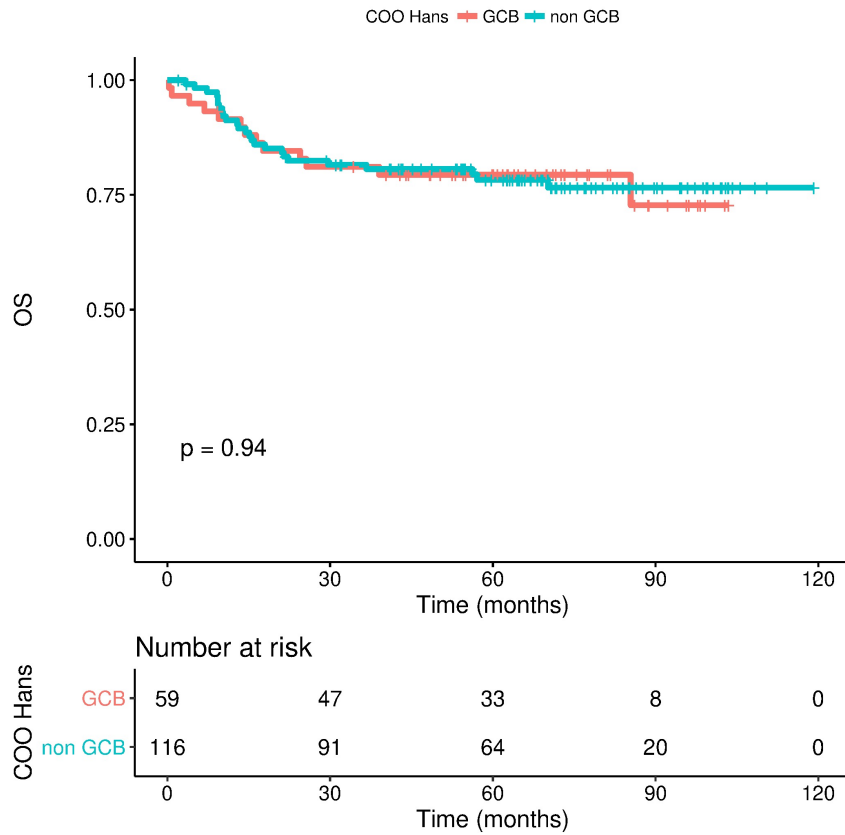
The mean age was 52 yr.s (18 – 65)

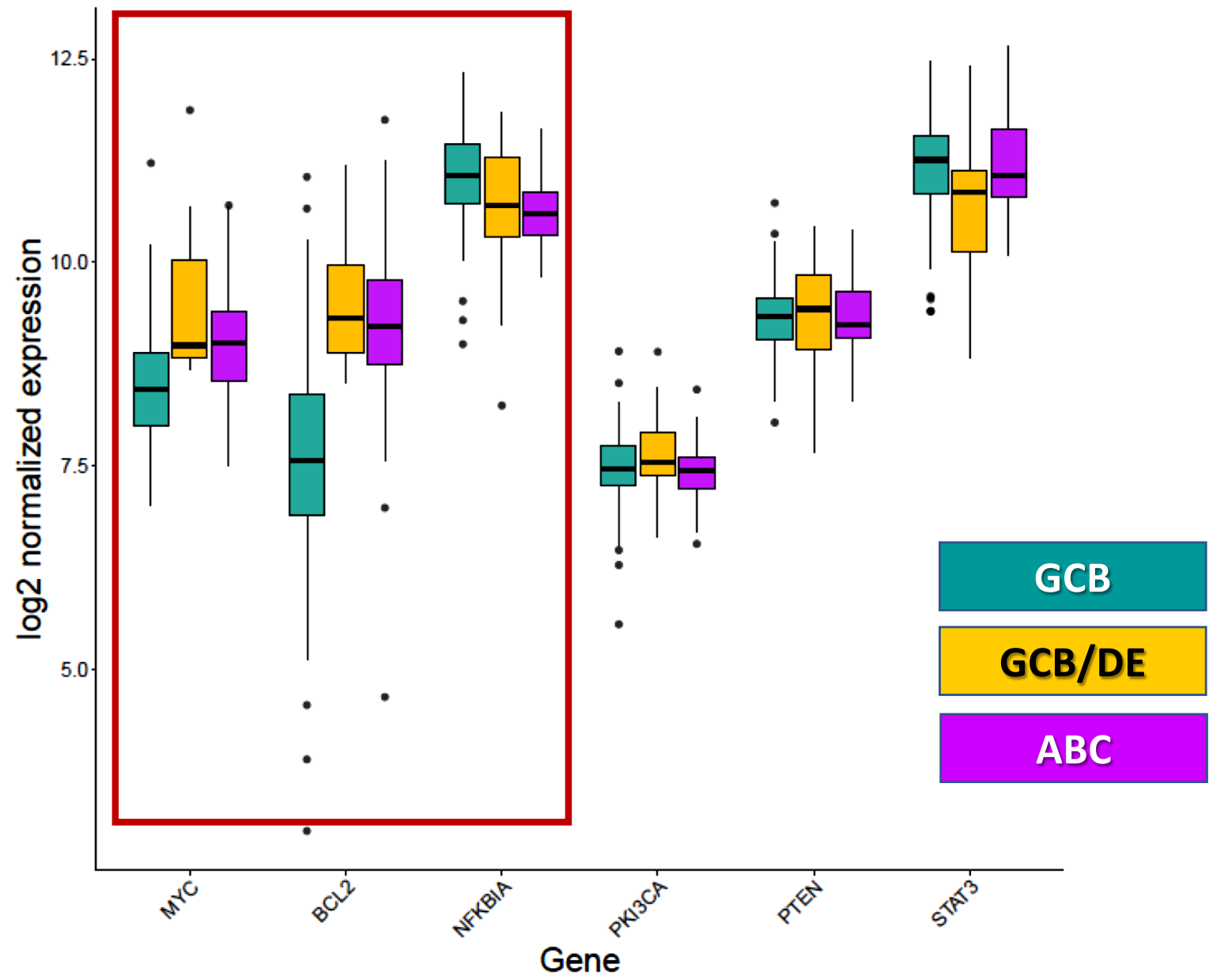
All the cases were studied by immunohistochemistry, targeted GEP and FISH (*BCL2*, *MYC* and *BCL6*).

COO according to targeted GEP

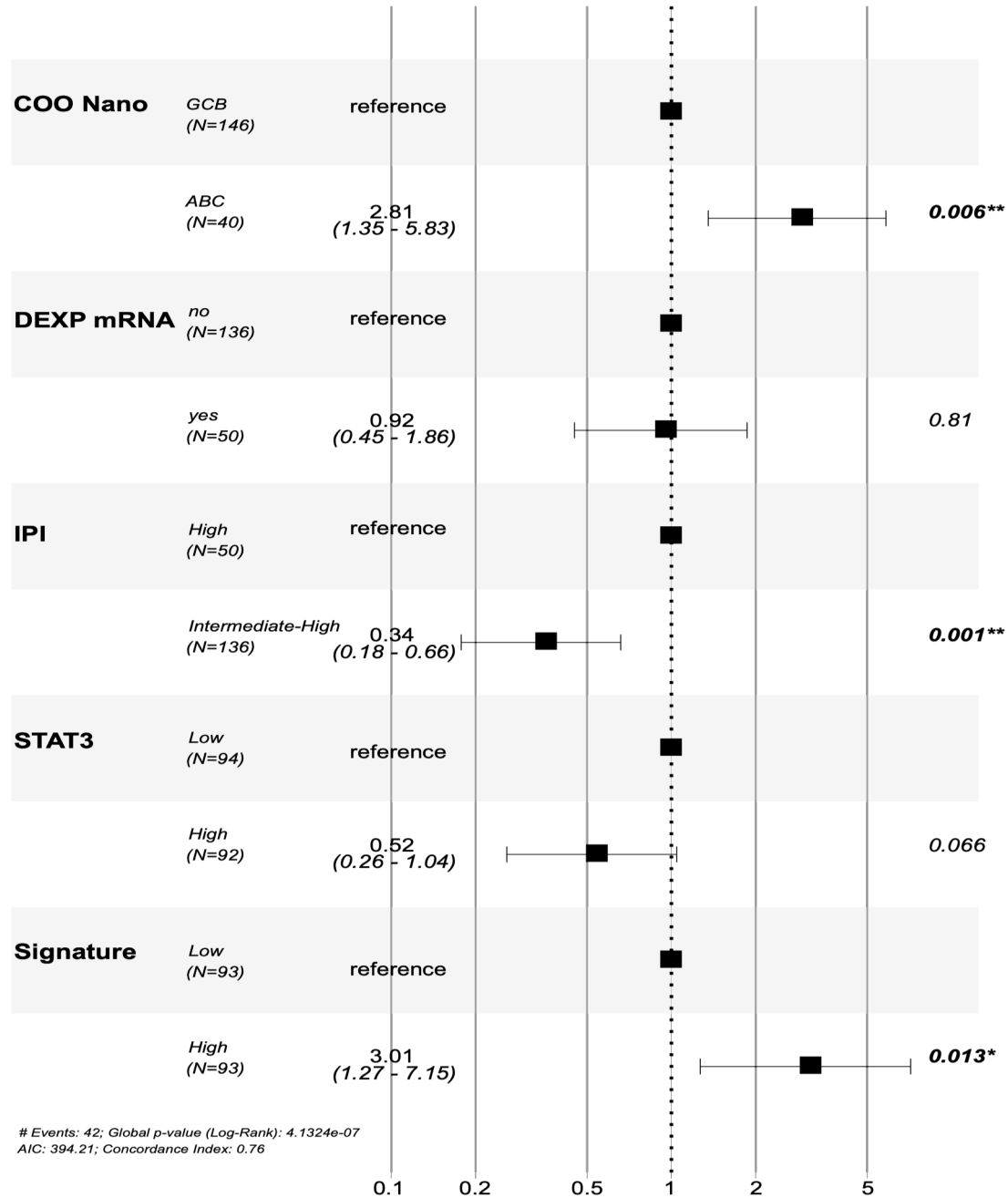


COO according to Hans' classifier

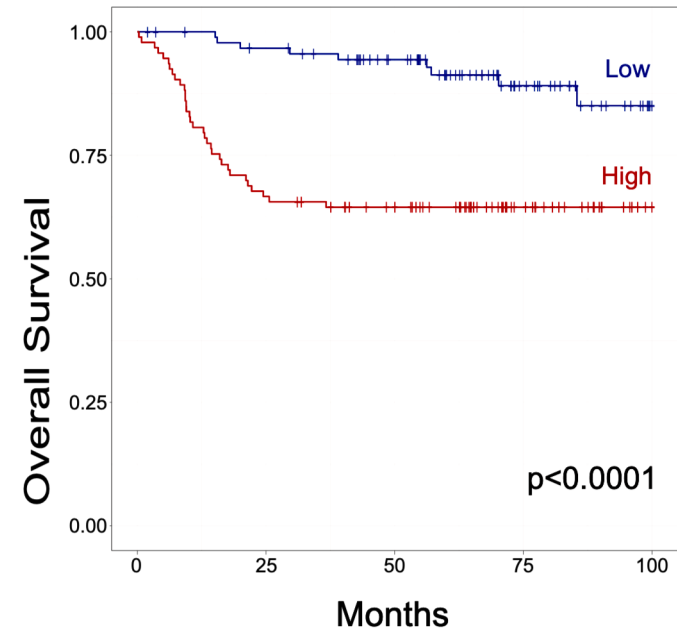




Variables **HR (95% CI)** **p-value**



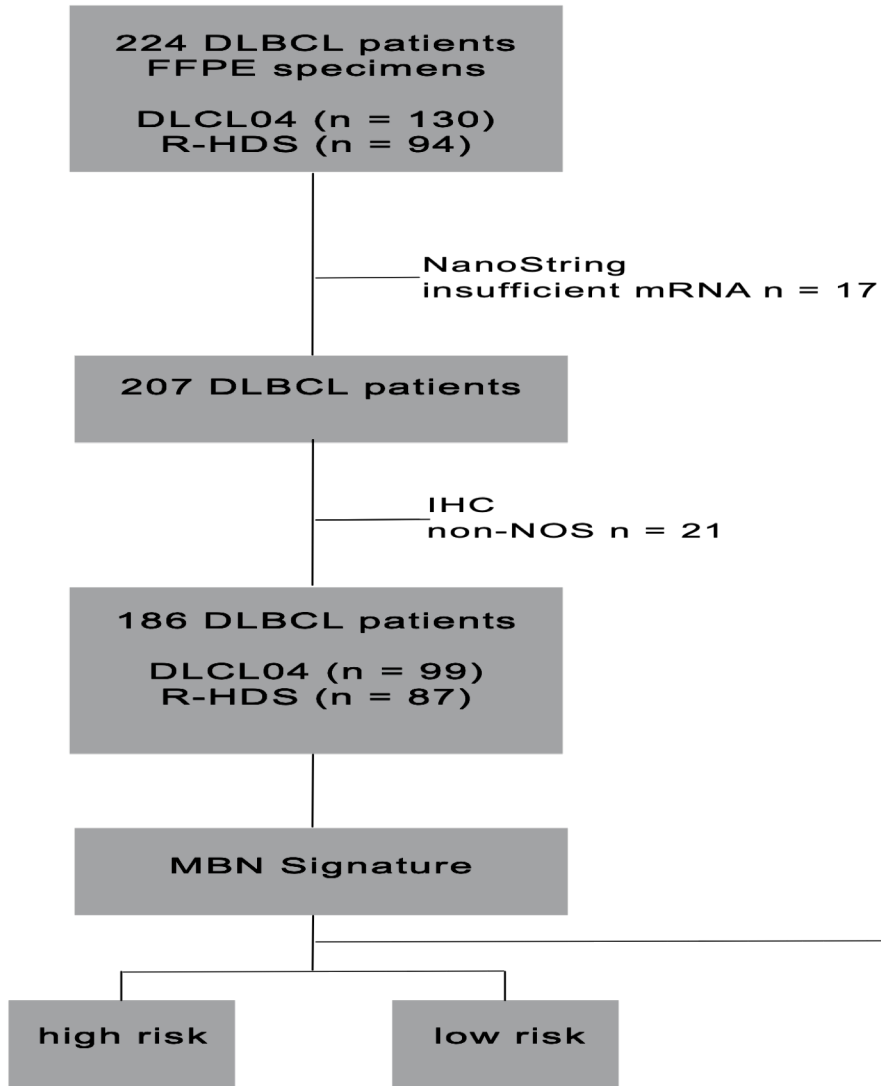
Events: 42; Global p-value (Log-Rank): 4.1324e-07
AIC: 394.21; Concordance Index: 0.76



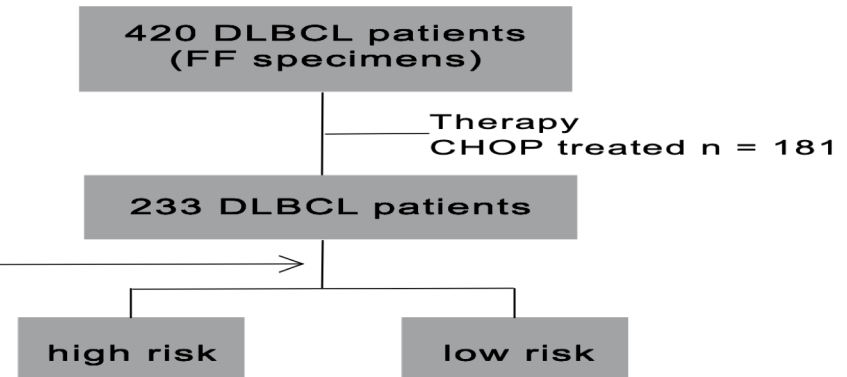
Groups	0	25	50	75	100
Low	93	86	70	34	10
High	93	62	52	23	3

Molecular High-Grade B-Cell Lymphoma: Defining a Poor-Risk Group That Requires Different Approaches to Therapy

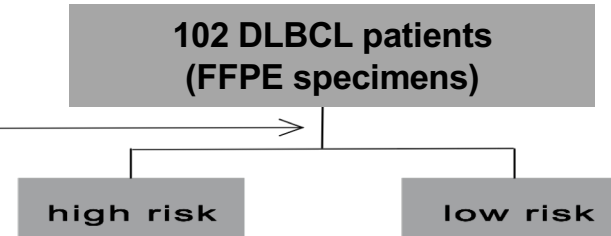
Chulin Sha, PhD¹; Sharon Barrans, PhD²; Francesco Cucco, PhD³; Michael A. Bentley, DPhil¹; Matthew A. Care, PhD¹; Thomas Cummin, MD⁴; Hannah Kennedy, PhD³; Joe S. Thompson, MPhil³; Rahman Uddin, MSc¹; Lisa WorriIlow, PhD²; Rebecca Chalkley, MPhil²; Moniek van Hoppe, MSc²; Sophia Ahmed, PhD¹; Tom Maishman, PhD⁴; Josh Caddy, BSc⁴; Anna Schuh, MD⁵; Christoph Mamot, MD⁶; Catherine Burton, MD²; Reuben Tooze, PhD¹; Andrew Davies, PhD⁴; Ming-Qing Du, PhD³; Peter W.M. Johnson, MD⁴; and David R. Westhead, DPhil¹



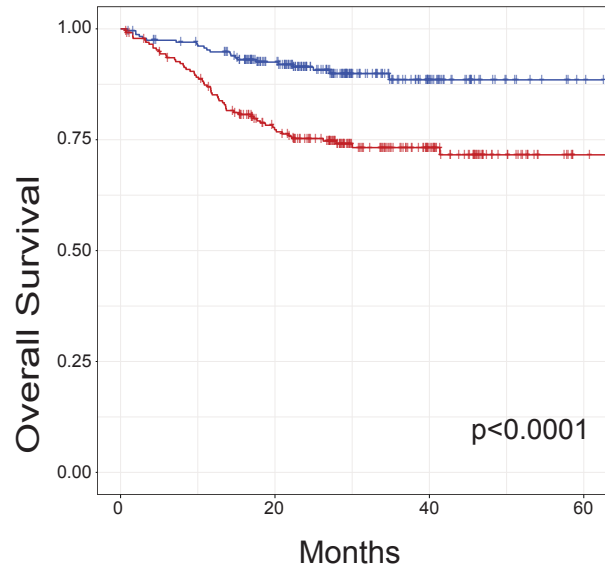
Validation Cohort (Lenz et al)



Validation Cohort (Real-life patients)

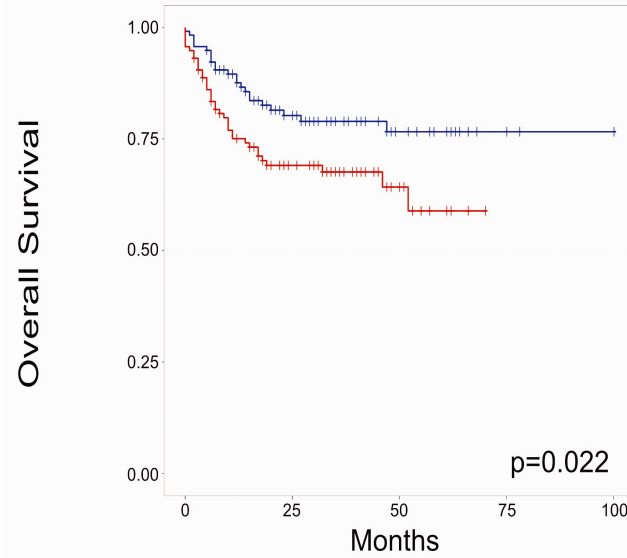


Sha's



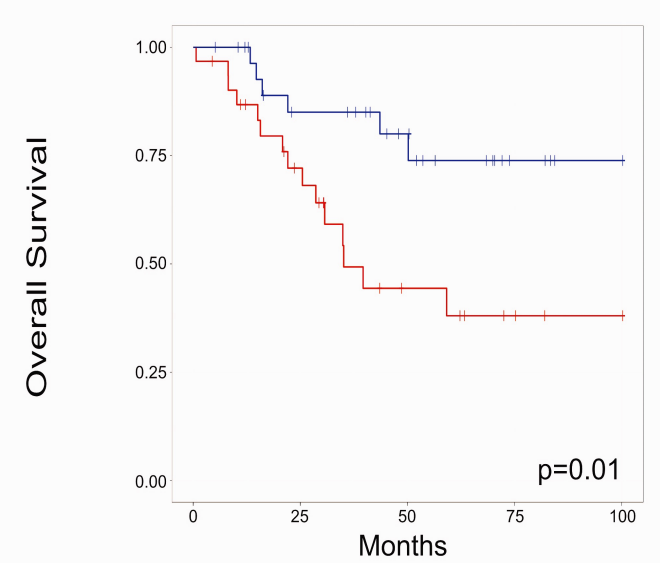
Groups	Low	High
Low	235	174
High	234	156

Lenz's



Groups	MBN Low	MBN High
MBN Low	117	66
MBN High	116	54

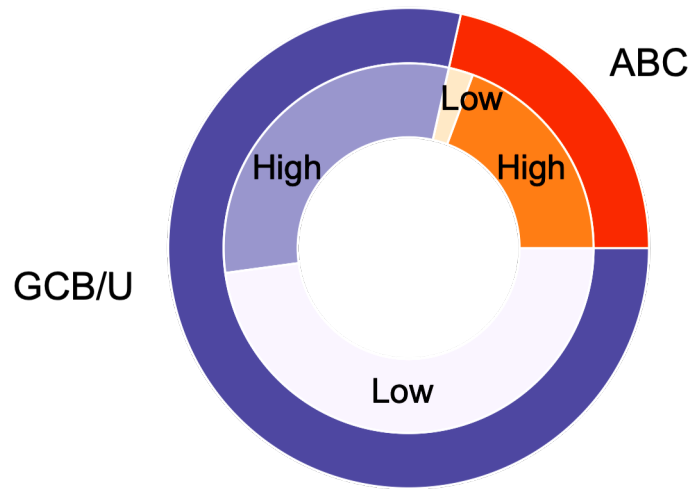
Real-life



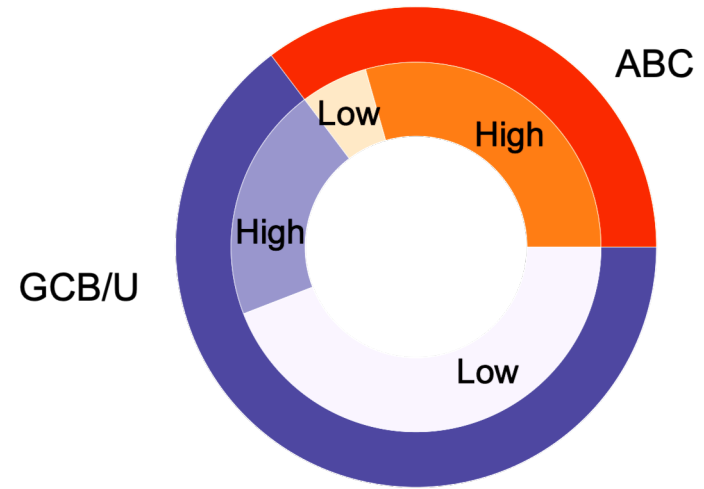
Groups	MBN Low	MBN High
MBN Low	31	21
MBN High	31	18

R-CHOP

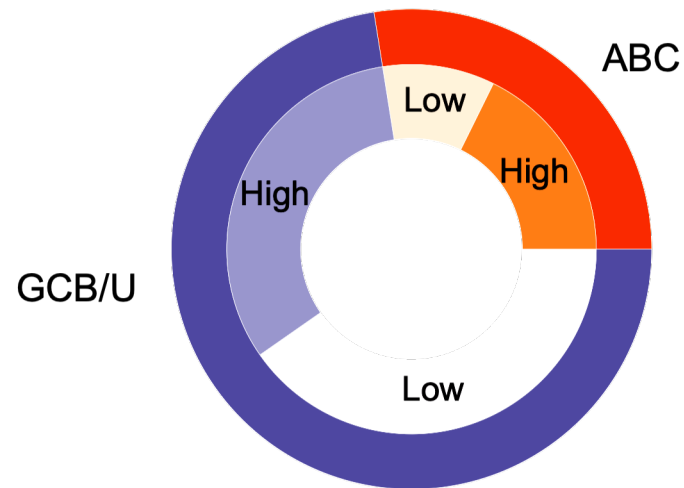
TRIALS n = 186

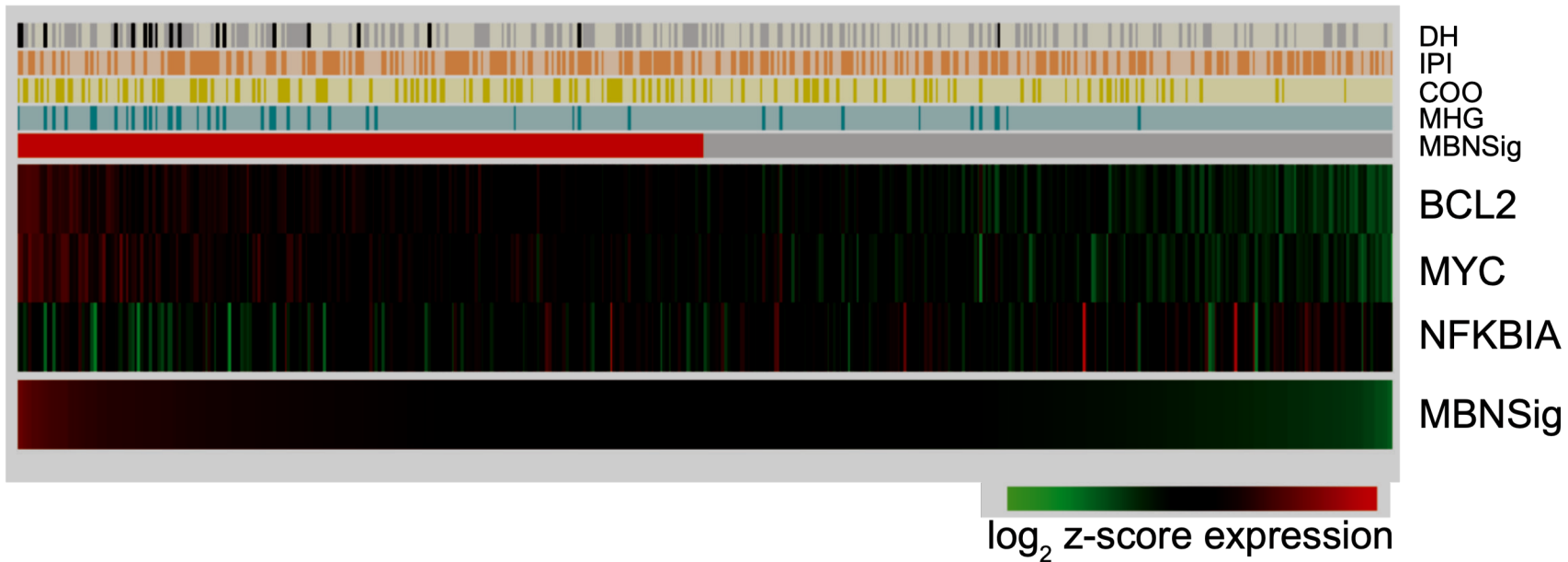


REAL-LIFE n = 102



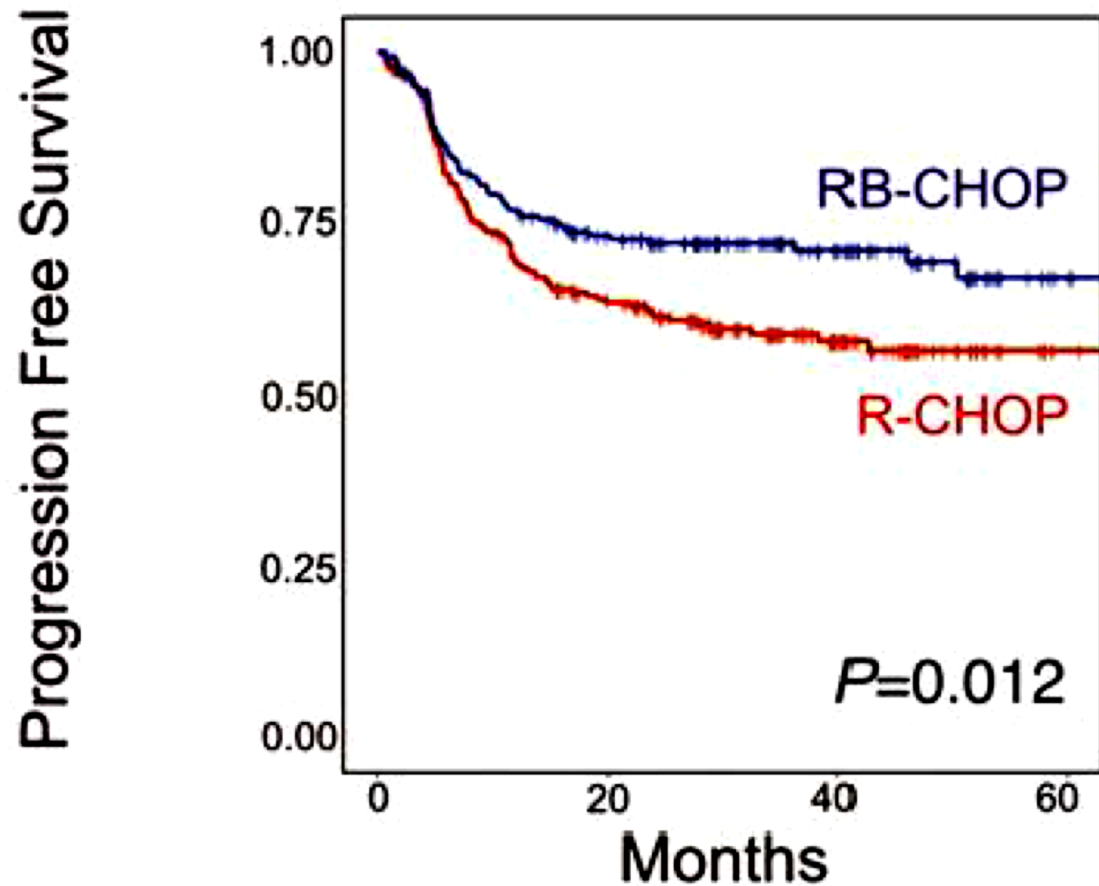
SHA COHORT n = 469





MBNSig	■ Positive	■ Negative	
MHG	■ MHG	■ Not MHG	
COO	■ ABC	■ Not ABC	
IPI	■ High	■ Low	
DH	■ Positive	■ Negative	■ NA

Patients from Sha's series with high MBN



Groups	R-CHOP	231	132	50	2
	RB-CHOP	233	142	59	5

Conclusions

- **The MBN signature does implement the cell of origin (COO) determination.**
- **A higher risk group (enriched in genetic aberrations) can be identified among GCB/U and ABC DLBCLs.**
- **Potential therapeutic implications.**
- **Applicable to all patients at low cost!!!**

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

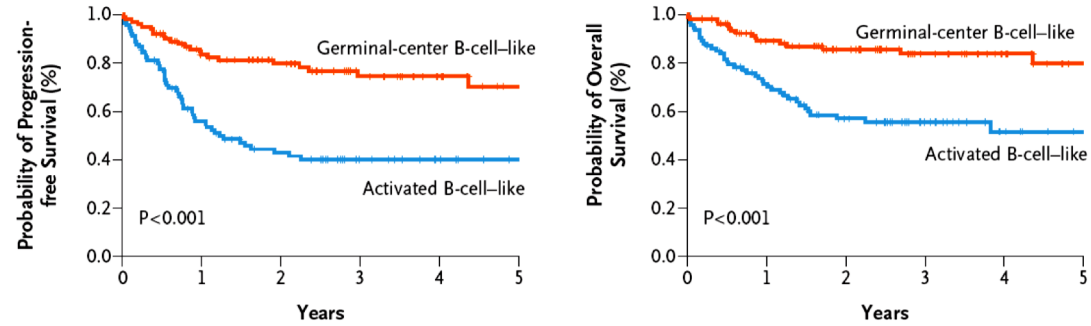
NOVEMBER 27, 2008

VOL. 359 NO. 22

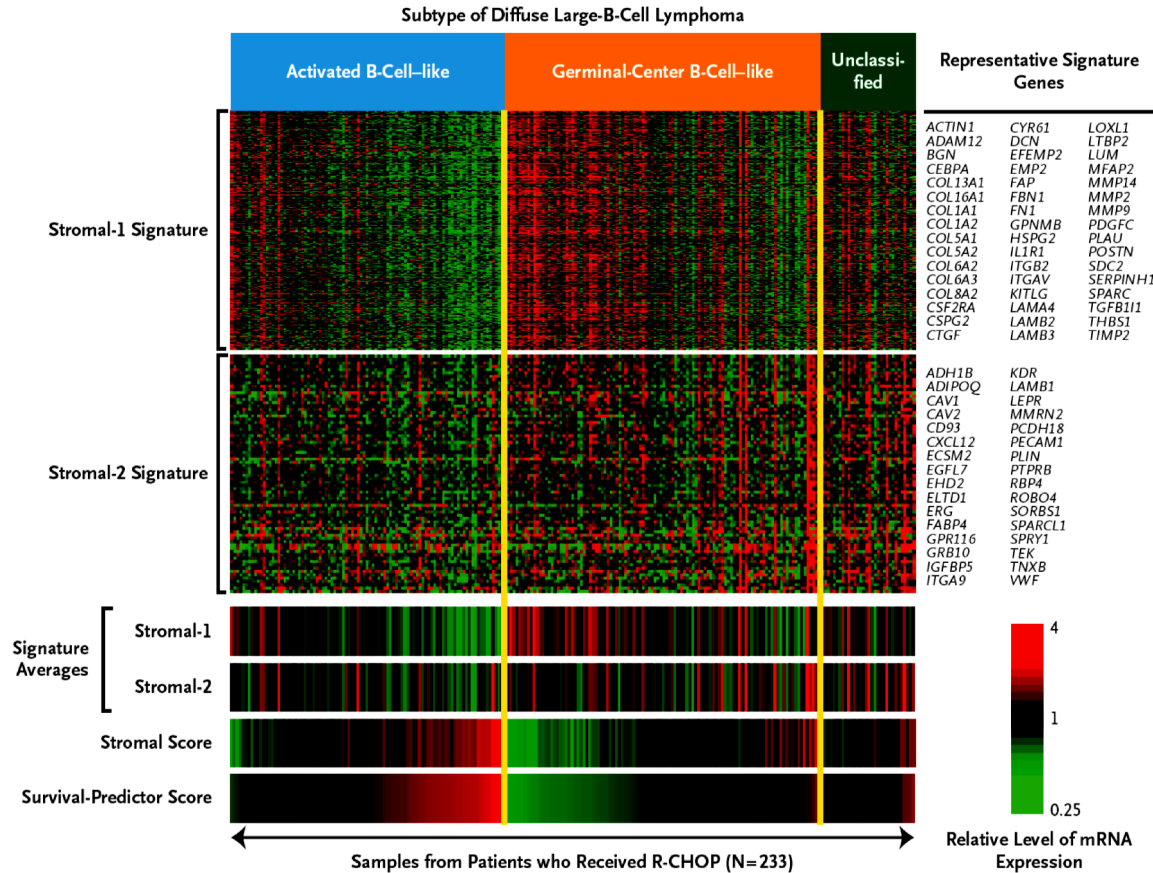
Stromal Gene Signatures in Large-B-Cell Lymphomas

G. Lenz, M.D., G. Wright, Ph.D., S.S. Dave, M.D., W. Xiao, Ph.D., J. Powell, M.S., H. Zhao, M.S., W. Xu, M.S., B. Tan, M.D., N. Goldschmidt, M.D., J. Iqbal, Ph.D., J. Vose, M.D., M. Bast, B.S., K. Fu, M.D., Ph.D., D.D. Weisenburger, M.D., T.C. Greiner, M.D., J.O. Armitage, M.D., A. Kyle, Ph.D., L. May, Ph.D., R.D. Gascoyne, M.D., J.M. Connors, M.D., G. Troen, Ph.D., H. Holte, M.D., Ph.D., S. Kvaloy, M.D., Ph.D., D. Dierickx, M.D., G. Verhoef, M.D., J. Delabie, M.D., E.B. Smeland, M.D., Ph.D., P. Jares, Ph.D., A. Martinez, M.D., A. Lopez-Guillermo, M.D., E. Montserrat, M.D., E. Campo, M.D., R.M. Braziel, M.D., T.P. Miller, M.D., L.M. Rimsza, M.D., J.R. Cook, M.D., B. Pohlman, M.D., J. Sweetenham, M.D., R.R. Tubbs, M.D., R.I. Fisher, M.D., E. Hartmann, M.D., A. Rosenwald, M.D., G. Ott, M.D., H.-K. Muller-Hermelink, M.D., D. Wrench, M.D., T.A. Lister, M.D., E.S. Jaffe, M.D., W.H. Wilson, M.D., Ph.D., W.C. Chan, M.D., and L.M. Staudt, M.D., Ph.D.,
for the Lymphoma/Leukemia Molecular Profiling Project

A



No. at Risk		0	1	2	3	4	5
Germinal-center B-cell-like	107	82	61	39	27	15	
Activated B-cell-like	93	60	38	23	11	6	



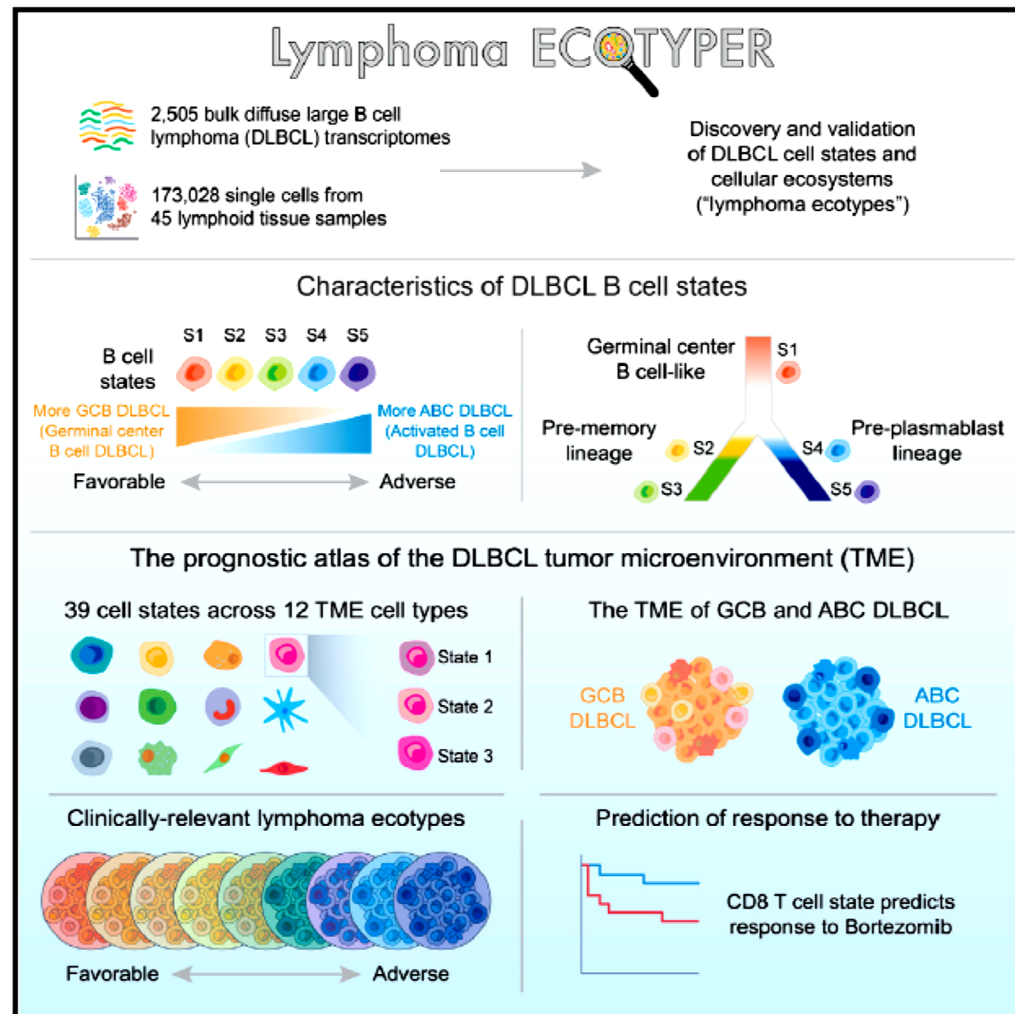
Stromal-1:
Extra-cellular matrix
deposition +
Macrophage
infiltration

Stromal-2:
Angiogenic genes
→
Micro-vessel
density

Cancer Cell

The landscape of tumor cell states and ecosystems in diffuse large B cell lymphoma

Graphical abstract



Authors

Chloé B. Steen, Bogdan A. Luca, Mohammad S. Esfahani, ..., Andrew J. Gentles, Aaron M. Newman, Ash A. Alizadeh

Correspondence

amnewman@stanford.edu (A.M.N.), arasha@stanford.edu (A.A.A.)

In brief

Steen et al. implement EcoTyper, a machine-learning approach for dissecting cellular heterogeneity in the most common blood cancer, diffuse large B cell lymphoma (DLBCL). Forty-four cell states spanning malignant cells and the microenvironment are defined, uncovering a rich landscape of cellular ecosystems that extend beyond traditional DLBCL classifications, revealing new opportunities for therapy selection.

ACCEPTED MANUSCRIPT

Dissection of DLBCL Microenvironment Provides a Gene Expression-Based Predictor of Survival Applicable to Formalin-Fixed Paraffin-Embedded Tissue

S Ciavarella, M C Vegliante, M Fabbri, S De Summa, F Melle, G Motta, V De Iuliis, G Opinto, A Enjuanes, S Rega, A Gulino, C Agostinelli, A Scattone, S Tommasi, A Mangia, F Mele, G Simone, A F Zito, G Ingravallo, U Vitolo, A Chiappella, C Tarella, A M Gianni, A Rambaldi, P L Zinzani, B Casadei, E Derenzini, G Loseto, A Pileri, V Tabanelli, S Fiori, A Rivas-Delgado, A López-Guillermo, T Venesio, A Sapino, E Campo, C Tripodo, A Guarini, S A Pileri ✉

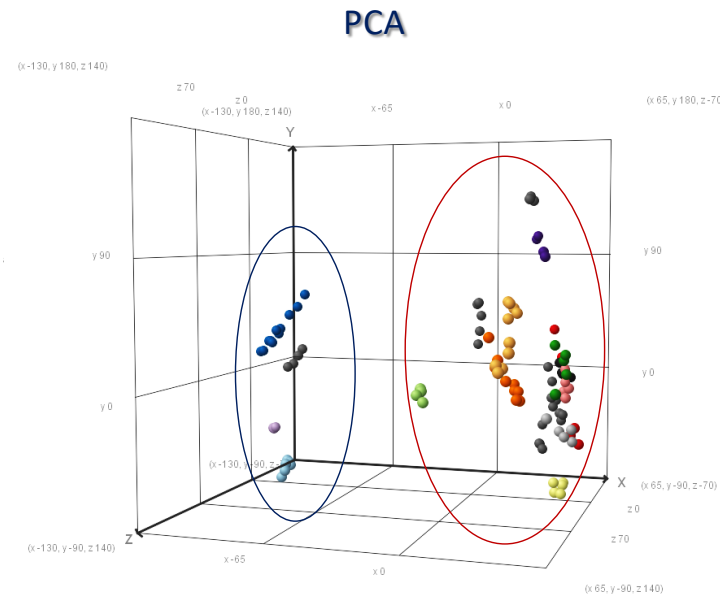
Annals of Oncology, mdy450, <https://doi.org/10.1093/annonc/mdy450>

Published: 11 October 2018

CIBERSORT analysis and selection of prognostic genes

A customized signature including 1,028 genes was generated to distinguish 17 cell types of both **stromal** and **immune** origin.

- Adipocites
- CD4-T cells
- CD8-T cells
- Dendritic cells
- Eosinophils
- Lymphatic endothelial cells
- Macrophages M2
- Memory_B_cells
- Monocytes
- Myofibroblasts
- NK_activated
- NK_resting
- Naive_B
- Neutrophils
- Pericytes
- Plasmacells
- Tgamma-delta



MF-related genes

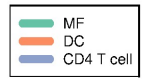
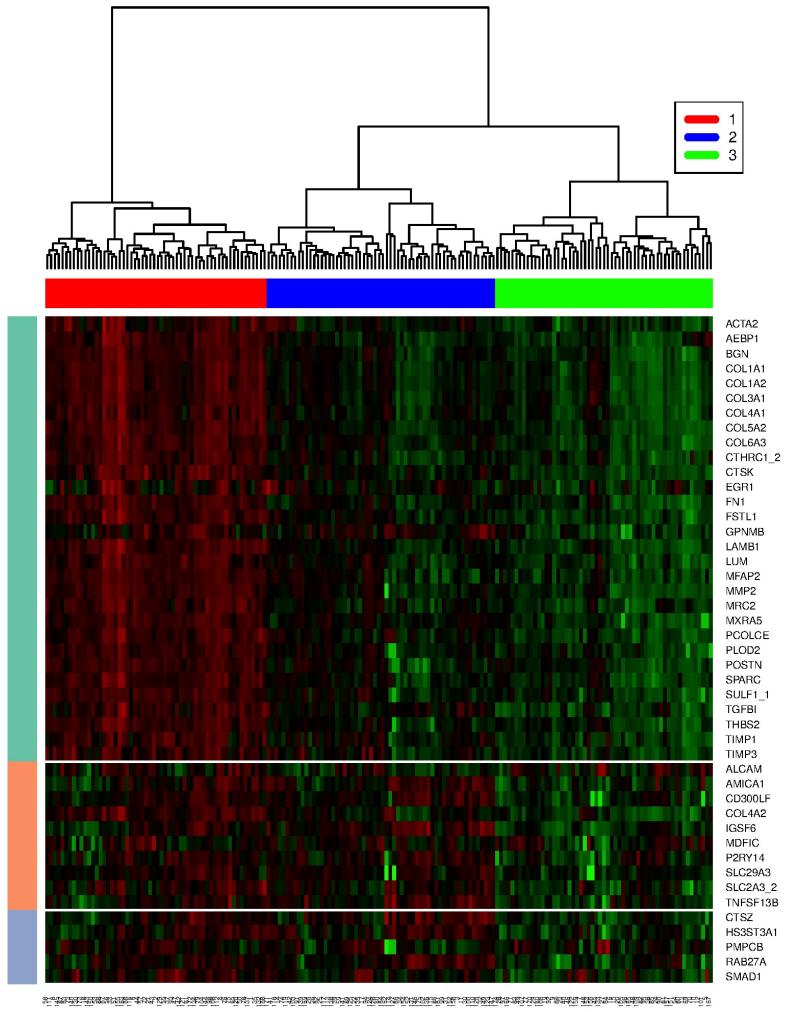
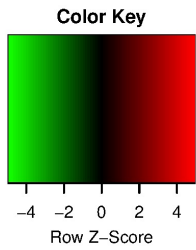
- ACTA2** Actin, alpha 2, smooth muscle
- AEBP1** AE binding protein 1
- BGN** Biglycan
- COL1A1** Collagen type I alpha 1
- COL1A2** Collagen type I alpha 2
- COL3A1** Collagen type III alpha 1
- COL4A1** Collagen type IV alpha 1
- COL5A2** Collagen type V alpha 2
- COL6A3** Collagen type VI alpha 3
- CTHRC1** Collagen triple helix repeat containing 1
- CTSK** Cathepsin K
- EGR1** Early growth response 1
- FN1** Fibronectin 1
- FSTL1** Follistatin like 1
- GNPMB** Glycoprotein nmb
- LAMB1** Laminin subunit beta 1
- LUM** Lumican
- MFAP2** Microfibrillar associated protein 2
- MMP2** Matrix metalloproteinase 2
- MRC2** Mannose receptor, C type 2
- MXRA5** Matrix-Remodelling Associated 5
- PCOLCE** Procollagen C-endopeptidase enhancer
- PLOD2** Procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2
- POSTN** Periostin, osteoblast specific factor
- SPARC** Secreted protein acidic and cysteine rich Sulfatase 1
- SULF1** Sulfatase 1
- TGFB1** Transforming growth factor beta induced

DC-related genes

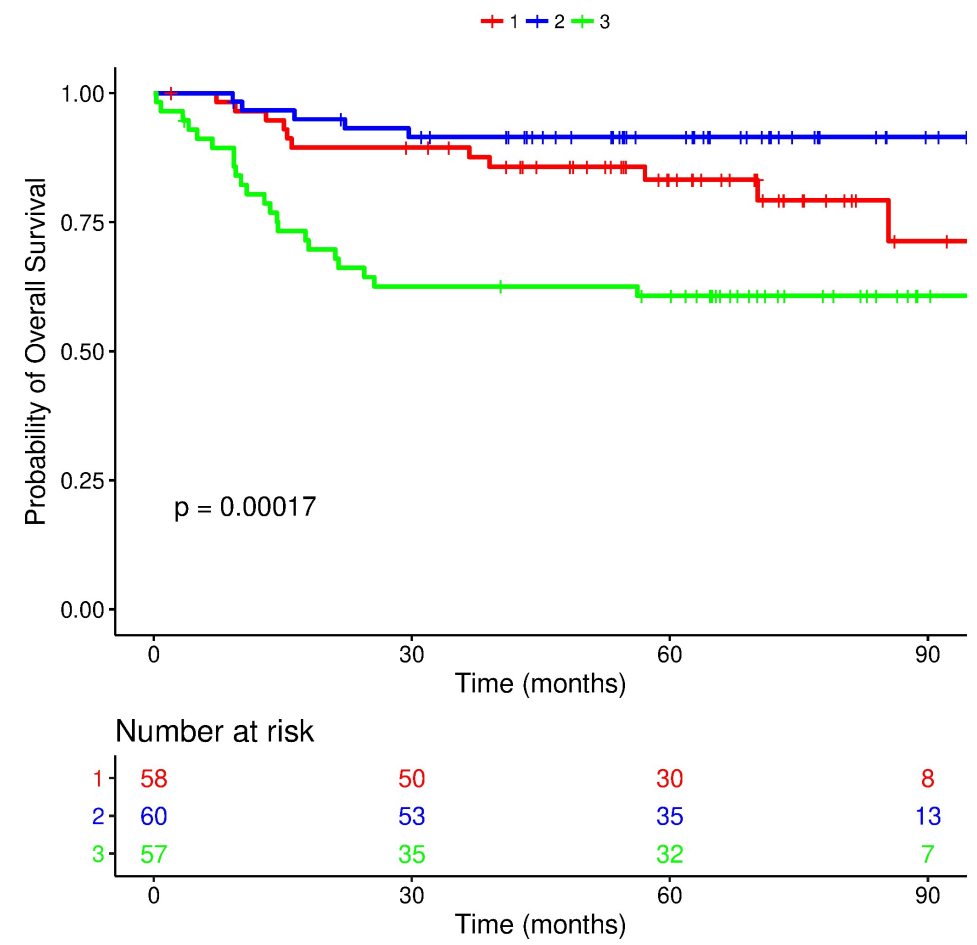
- ALCAM** Activated leukocyte cell adhesion molecule
- AMICA1** Adhesion molecule, interacts with CXADR antigen 1
- CD300LF** CD300 molecule-like family member F
- COL4A2** Collagen, type IV, alpha 2
- IGSF6** Immunoglobulin superfamily, member 6
- MDFIC** MyoD Family Inhibitor Domain Containing
- P2RY14** Purinergic receptor P2Y, G-protein coupled, 14
- SLC29A3** Solute carrier family 29 (nucleoside transporters), member 3;
- SLC2A3** Solute carrier family 2 (facilitated glucose transporter),

CD4+ T cell-related genes

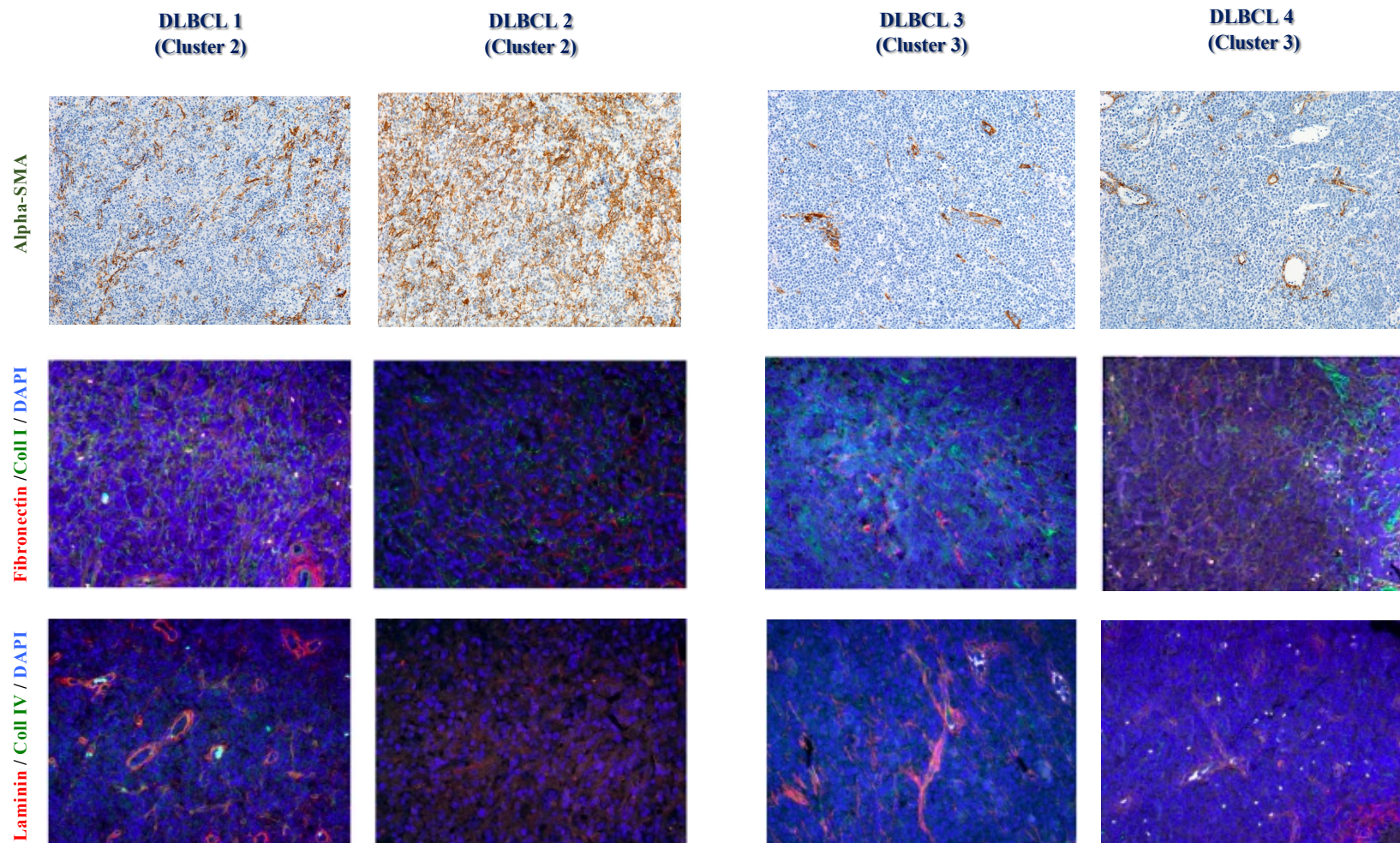
- CTSZ** Cathepsin Z
- HS3ST3A1** Heparan Sulfate-Glucosamine 3-Sulfotransferase 3A1
- PMPCB** Peptidase, Mitochondrial Processing Beta Subunit
- RAB27A** RAB27A, Member RAS Oncogene Family
- SMAD1** SMAD Family Member 1

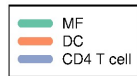
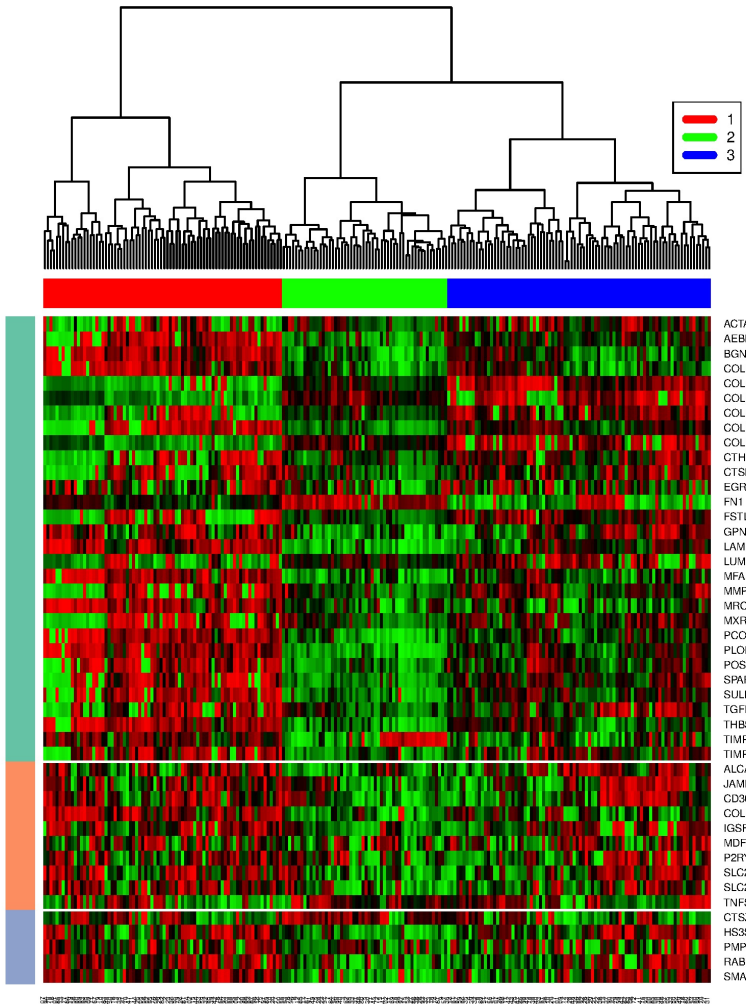
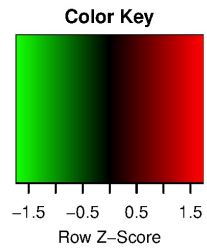


DLCL04 and R-HDS0305

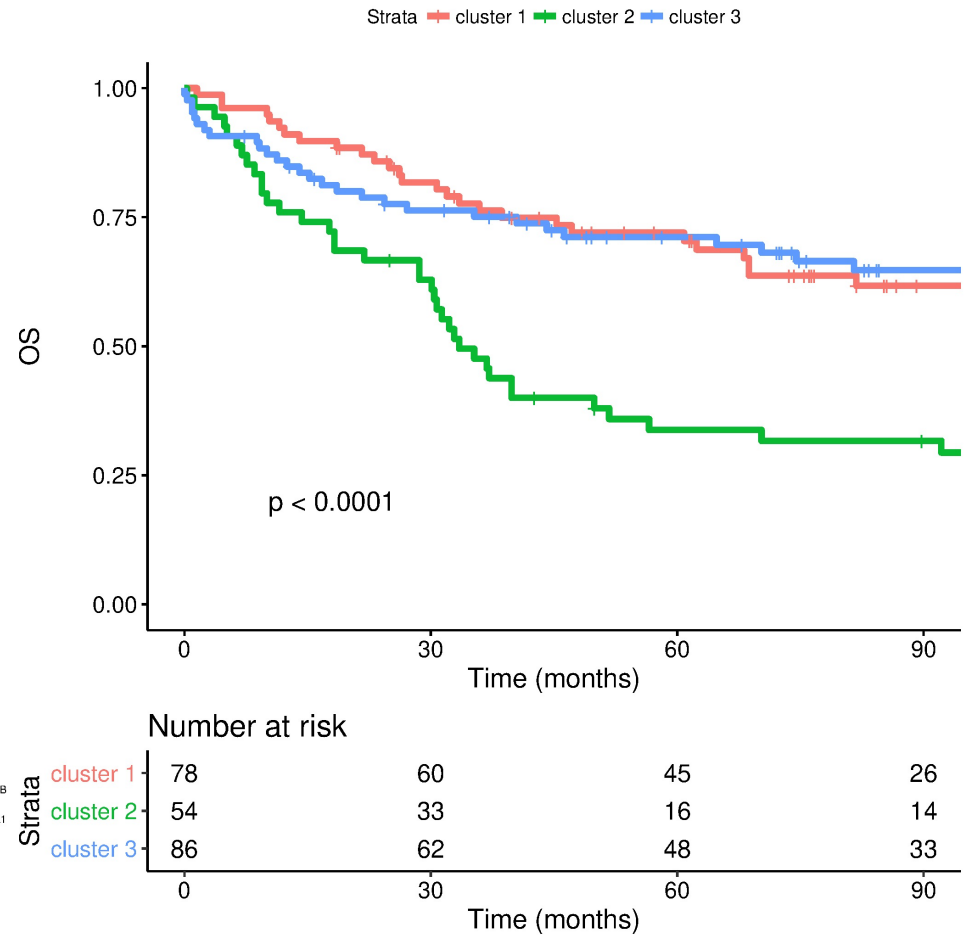


By *in situ* immunostaining we analyzed the expression of ECM proteins encoded by four of the fronting genes of the MF signature, namely Fibronectin, Collagen-I, Laminin, and Collagen-IV. However, the expression variability of these proteins does not support the use of immunohistochemistry as a reliable assay to provide insight on the prognostic gene expression patterns of DLBCL microenvironment determinants.



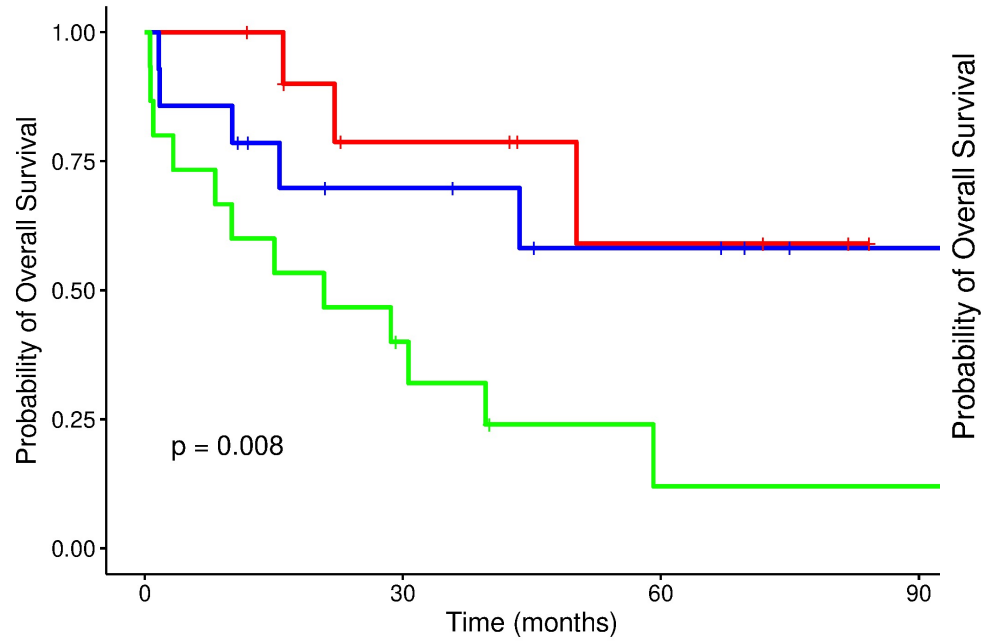


Lenz' series



Real-life

Cluster + 1 + 2 + 3

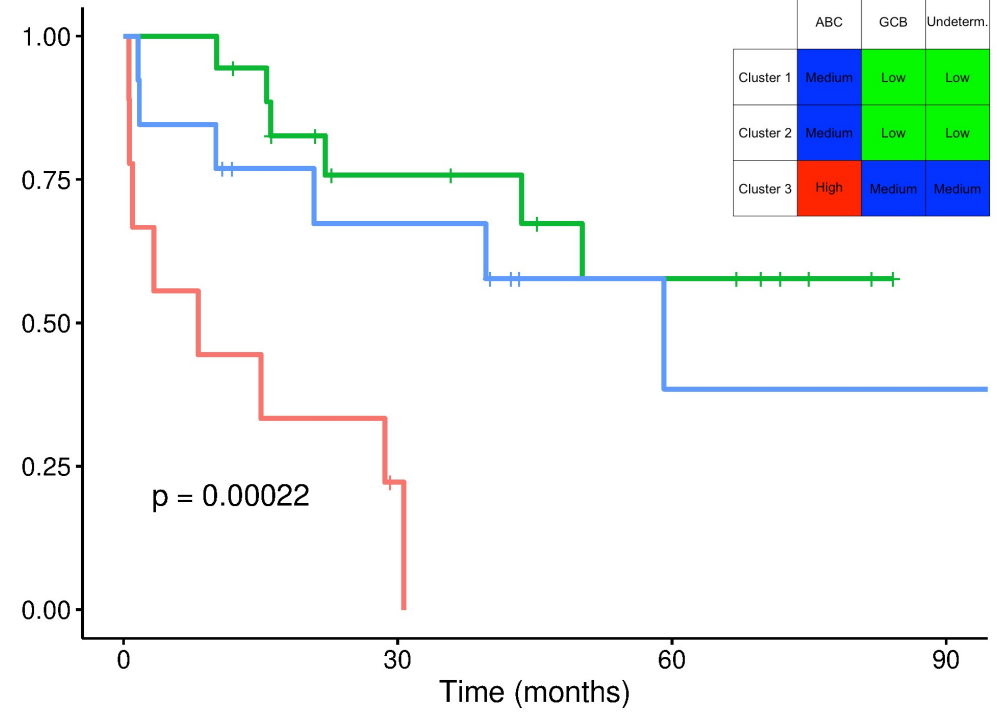


Cluster	Number at risk			
	0	30	60	90
1	11	6	3	0
2	14	7	4	1
3	15	5	1	1

Time (months)

Risk + High + Low + Medium

	Risk Index		
	ABC	GCB	Undeterm.
Cluster 1	Medium	Low	Low
Cluster 2	Medium	Low	Low
Cluster 3	High	Medium	Medium



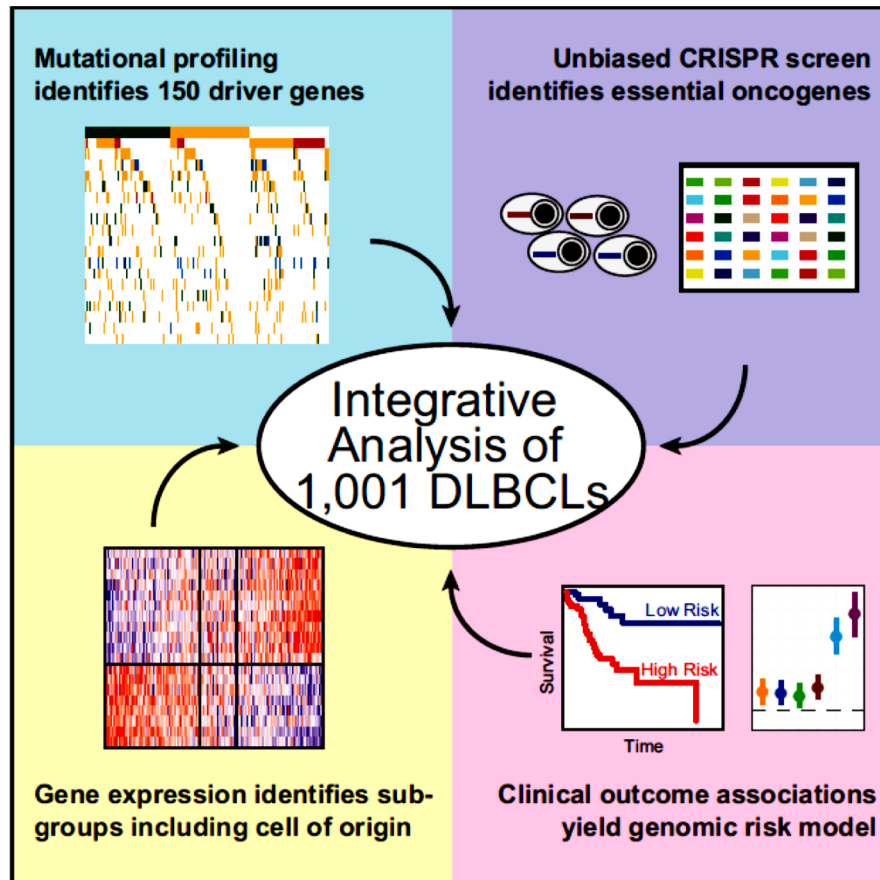
Risk	Number at risk			
	0	30	60	90
High	9	1	0	0
Low	18	10	6	0
Medium	13	7	2	2

Time (months)

Next generation sequencing

Genetic and Functional Drivers of Diffuse Large B Cell Lymphoma

Graphical Abstract



Authors

Anupama Reddy, Jenny Zhang,
Nicholas S. Davis, ..., Jyotishka Datta,
David B. Dunson, Sandeep S. Dave

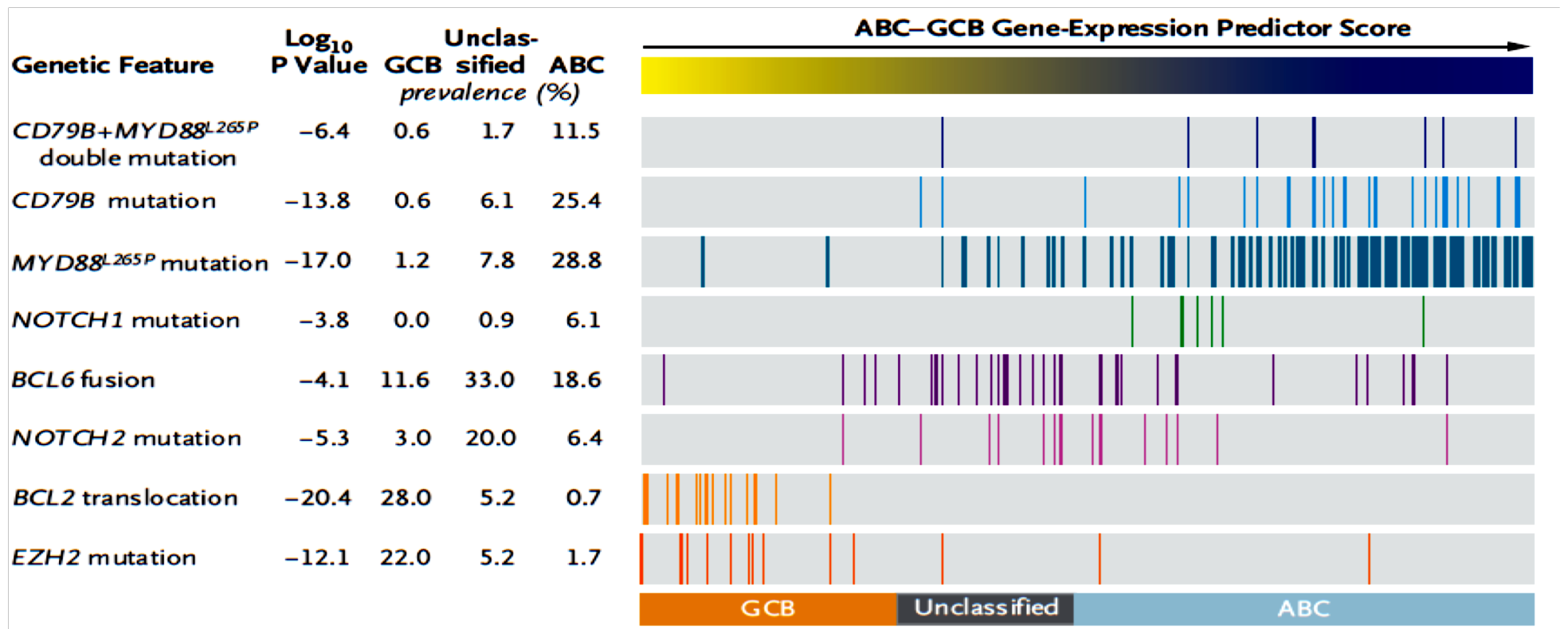
Correspondence

sandeep.dave@duke.edu

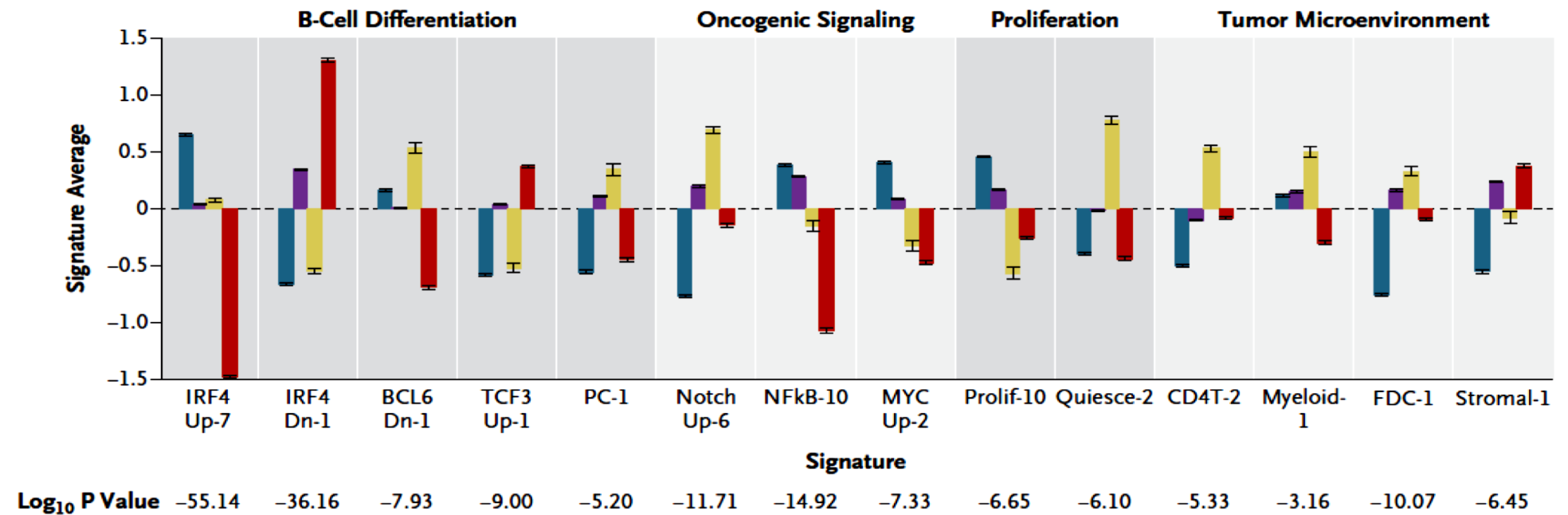
In Brief

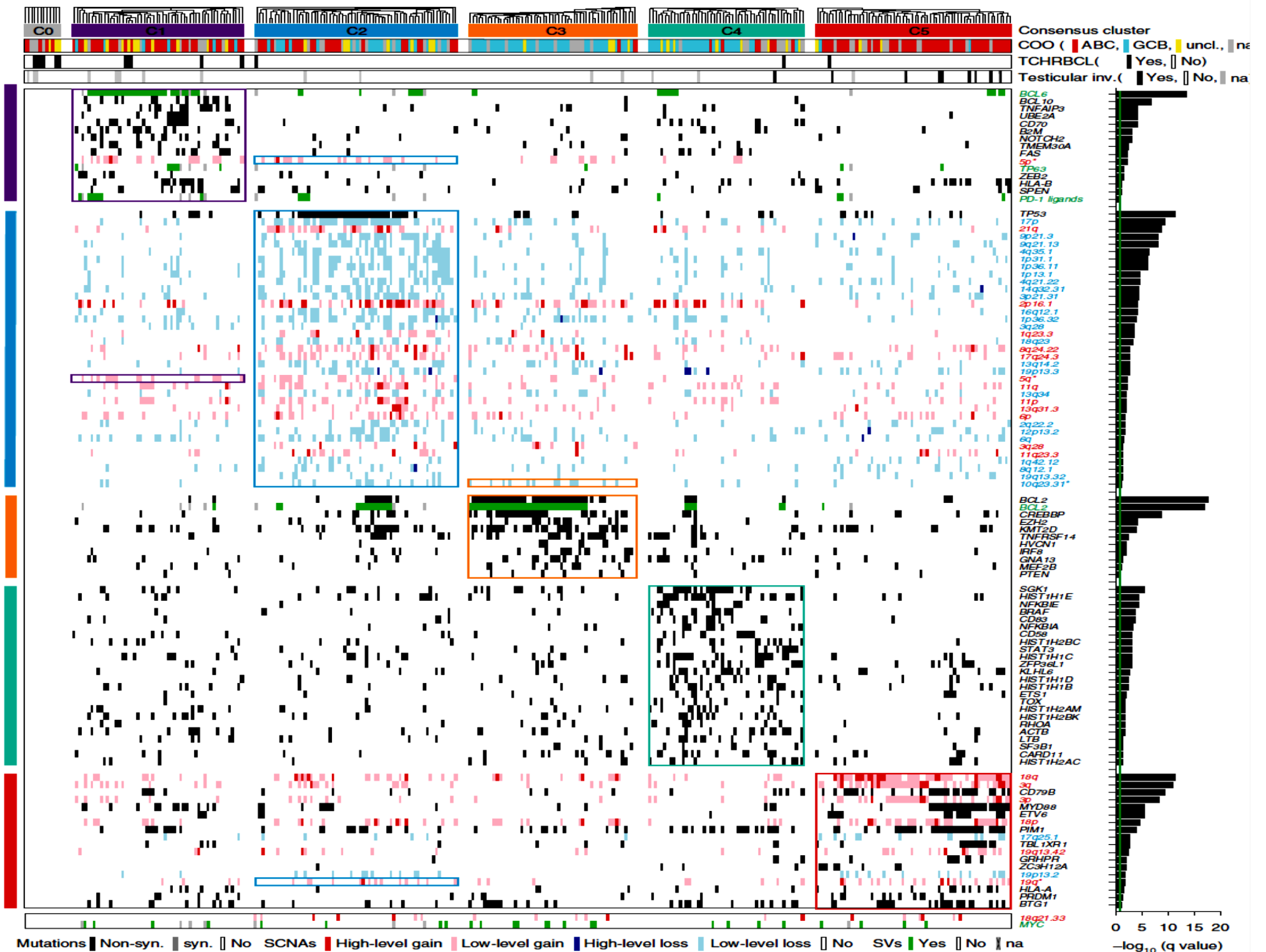
An integrative analysis in 1,001 newly diagnosed DLBCL patients identifies 150 genetic drivers with functional characterization using an unbiased CRISPR screen in DLBCL cell lines and connects with clinical outcome.

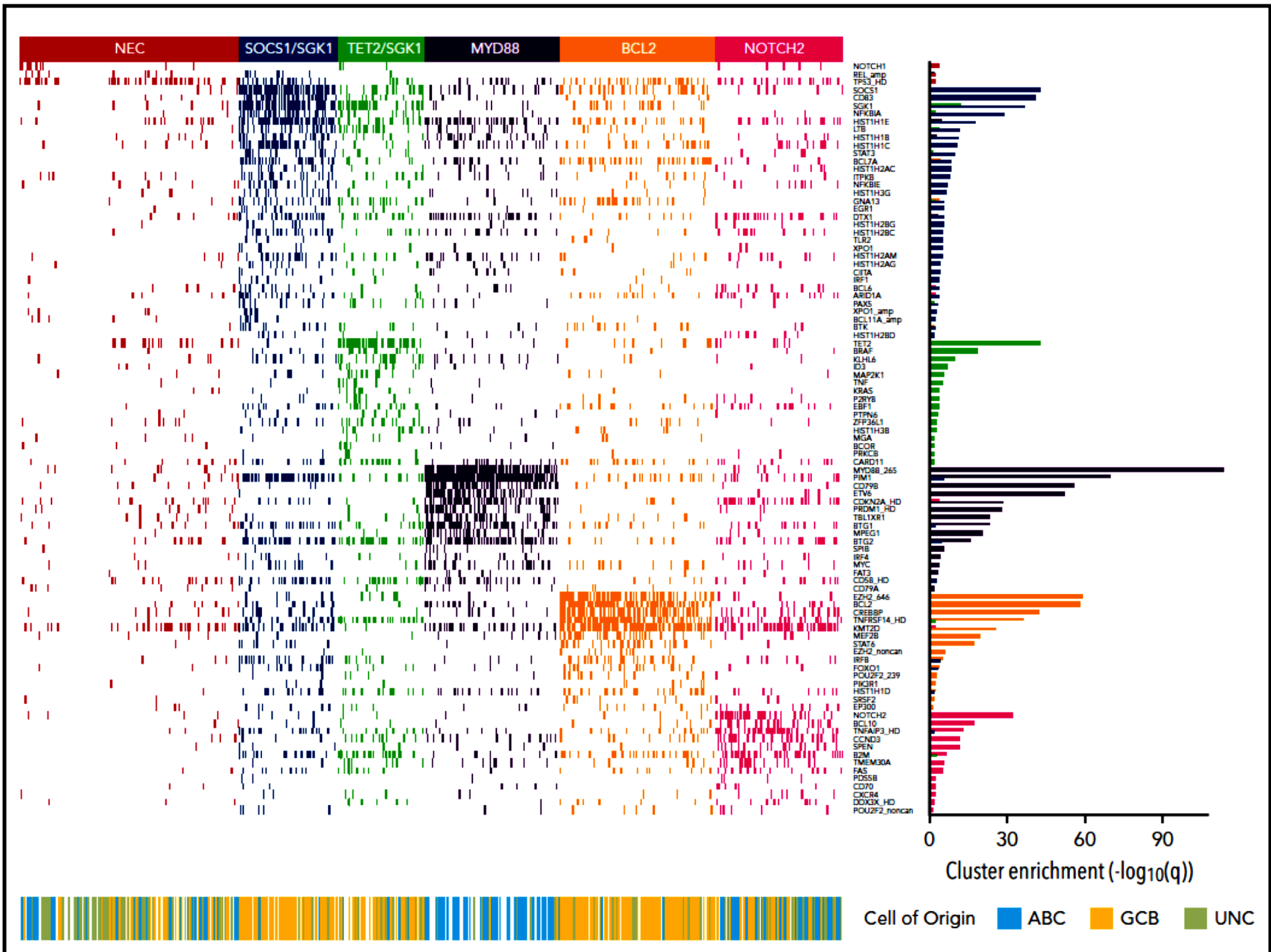
Cell 171, 481–494, October 5, 2017



■ MCD ■ BN2 ■ N1 ■ EZB



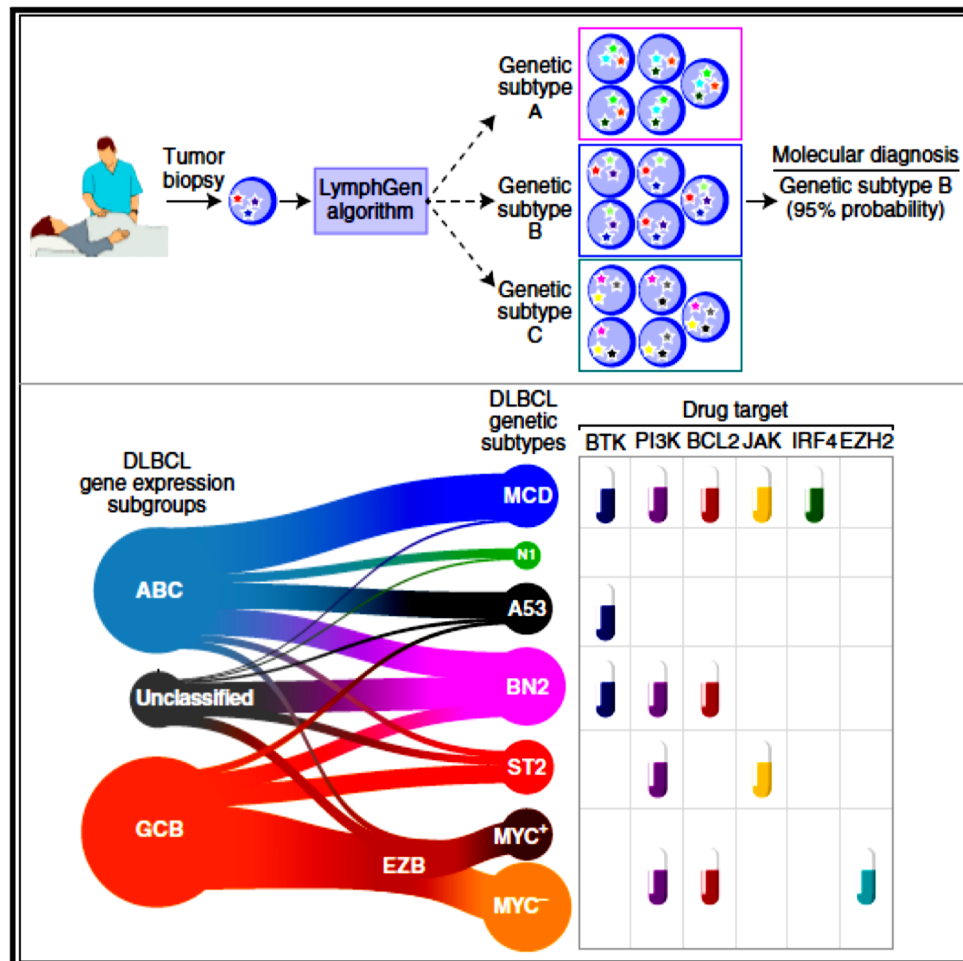




Cancer Cell

A Probabilistic Classification Tool for Genetic Subtypes of Diffuse Large B Cell Lymphoma with Therapeutic Implications

Graphical Abstract



Authors

George W. Wright, Da Wei Huang, James D. Phelan, ..., Wyndham H. Wilson, David W. Scott, Louis M. Staudt

Correspondence

lstaudt@mail.nih.gov

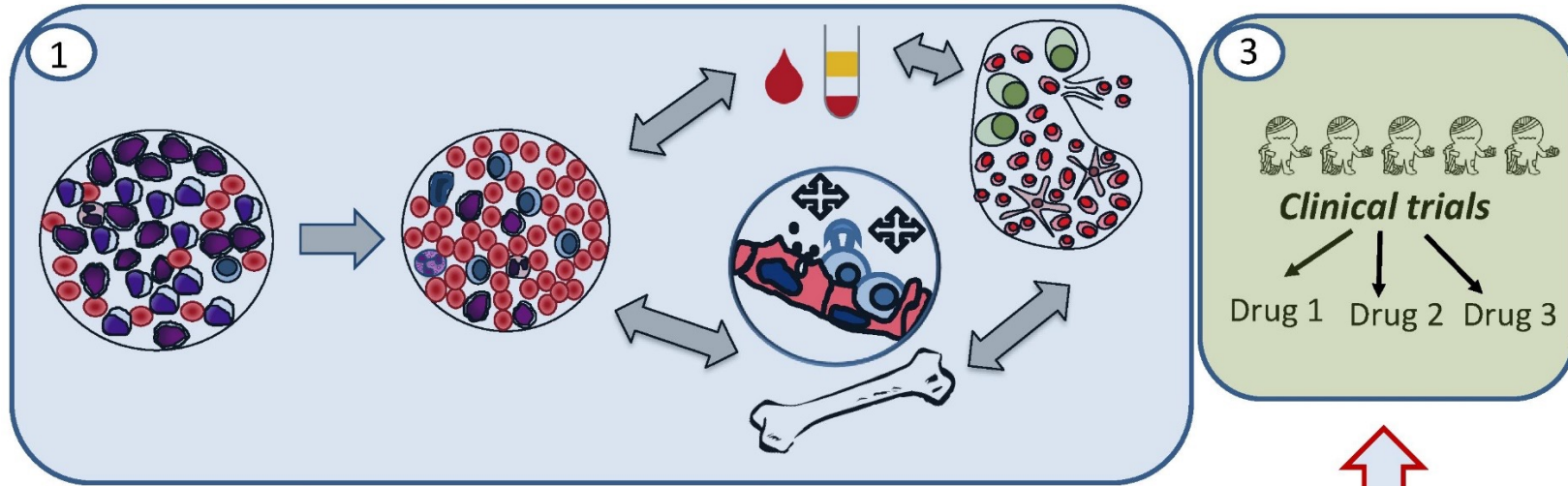
In Brief

Wright et al. identify seven genetic subtypes of diffuse large B cell lymphoma (DLBCL) with distinct outcomes and therapeutic vulnerabilities. The LymphGen probabilistic classification tool that can classify a DLBCL biopsy into the genetic subtypes is developed, which could be used for precision medicine trials.

Diagnosis

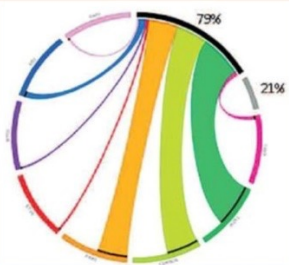
Resistance

Dissemination



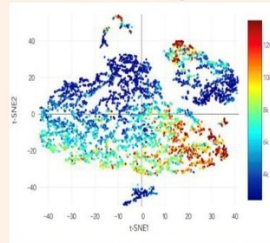
2

WES/RNAseq

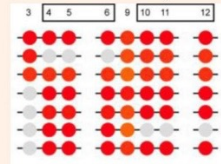


Target selection

scRNAseq

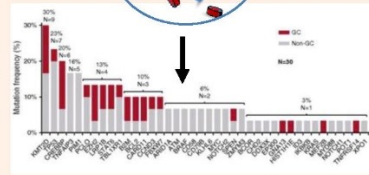
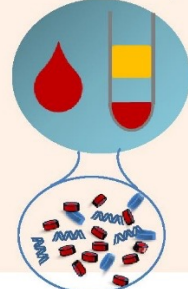


scBS-seq

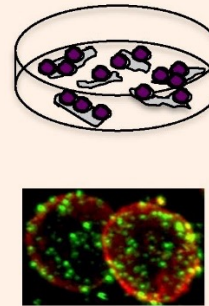


Platforms

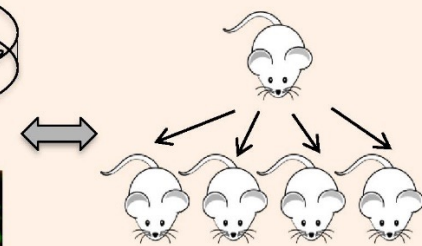
cfDNAseq



In vitro 2D/3D Models



Mouse Models

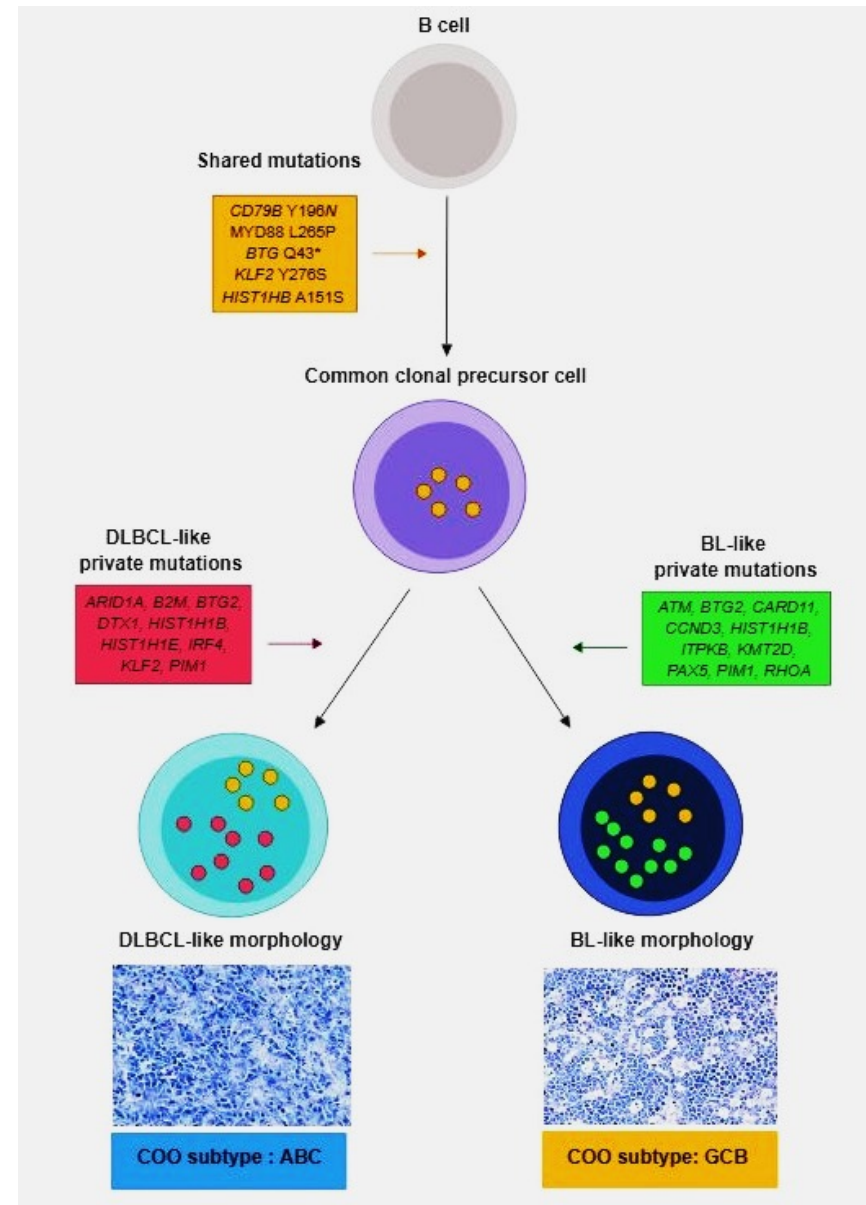


Drug screening

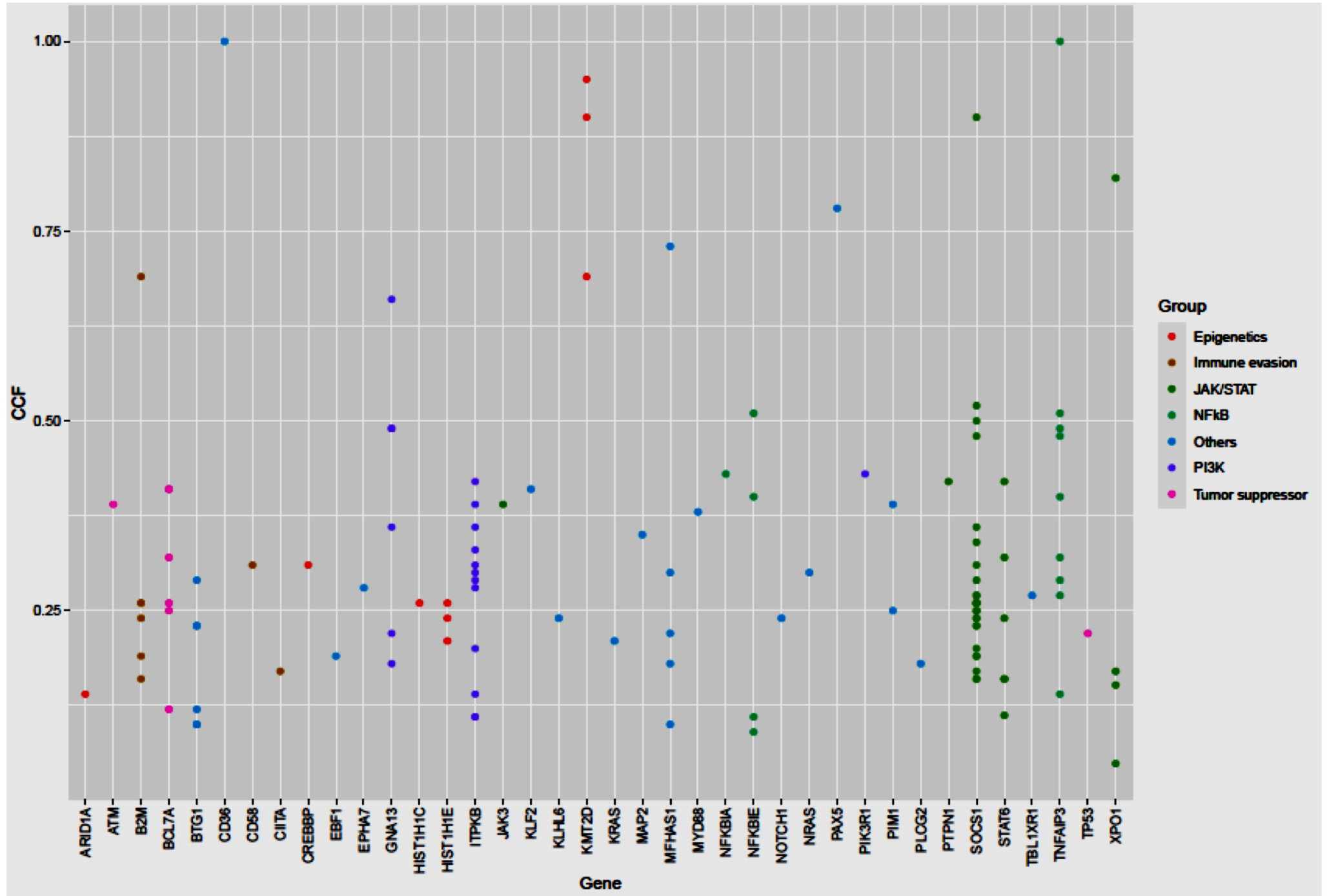
Evolutionary crossroads: morphological heterogeneity reflects divergent intra-clonal evolution in a case of high-grade B-cell lymphoma

by Valentina Tabanelli, Federica Melle, Giovanna Motta, Saveria Mazzara, Marco Fabbri, Chiara Corsini, Elvira Gerbino, Angelica Calleri, Maria Rosaria Sapienza, Ignazio Abbene, Viviana Stufano, Massimo Barberis, and Stefano A. Pileri

Haematologica 2020 [Epub ahead of print]



11 mediastinal GZLs (3 R/R) + 30 (EAHP Workshop)

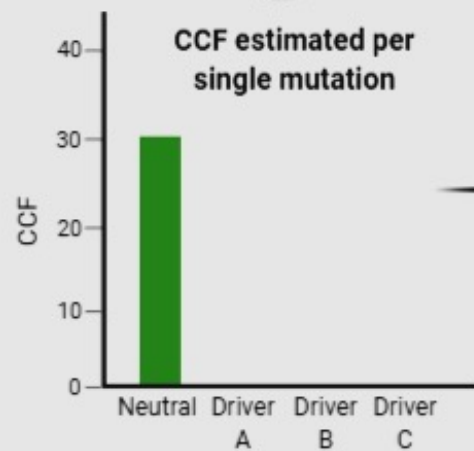
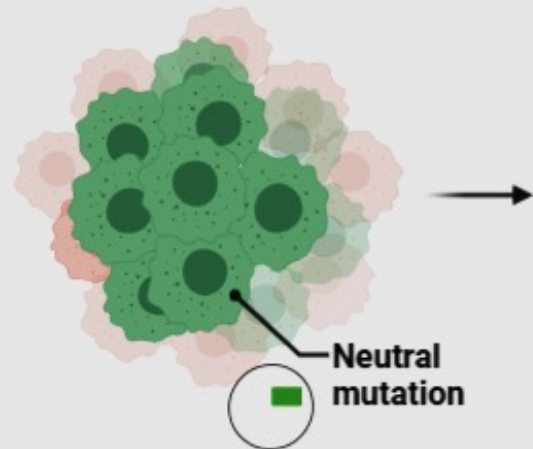


**Relapses due to subclonal
selection?**

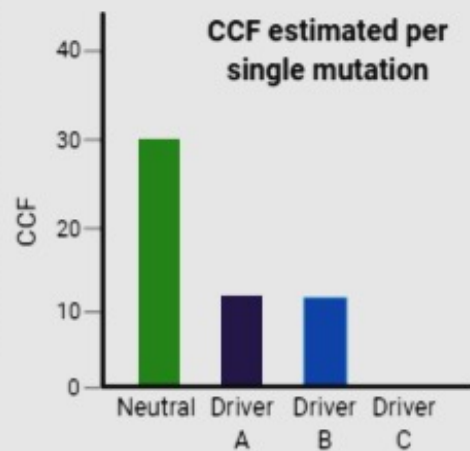
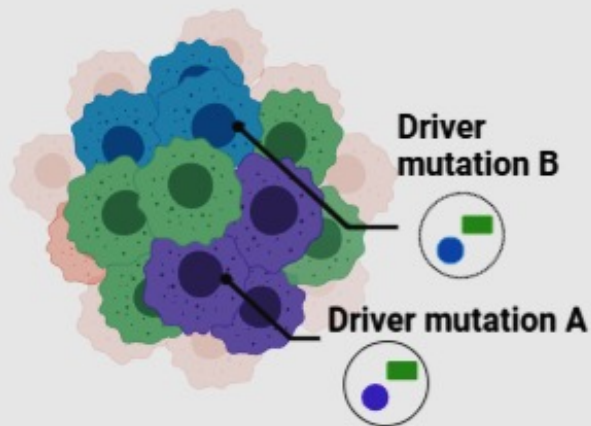
Primary GZL

Refractory/relapsed GZL

Neutral clone

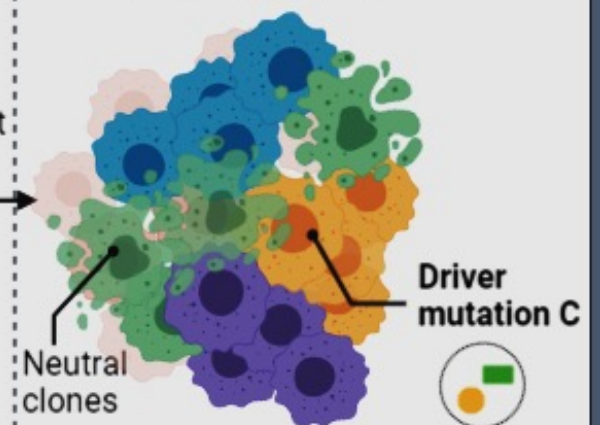


Emergence of driver clones

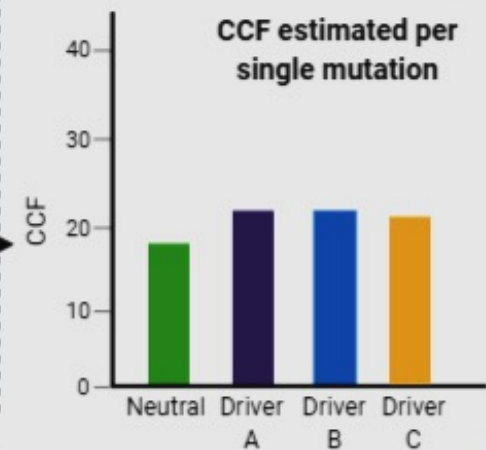


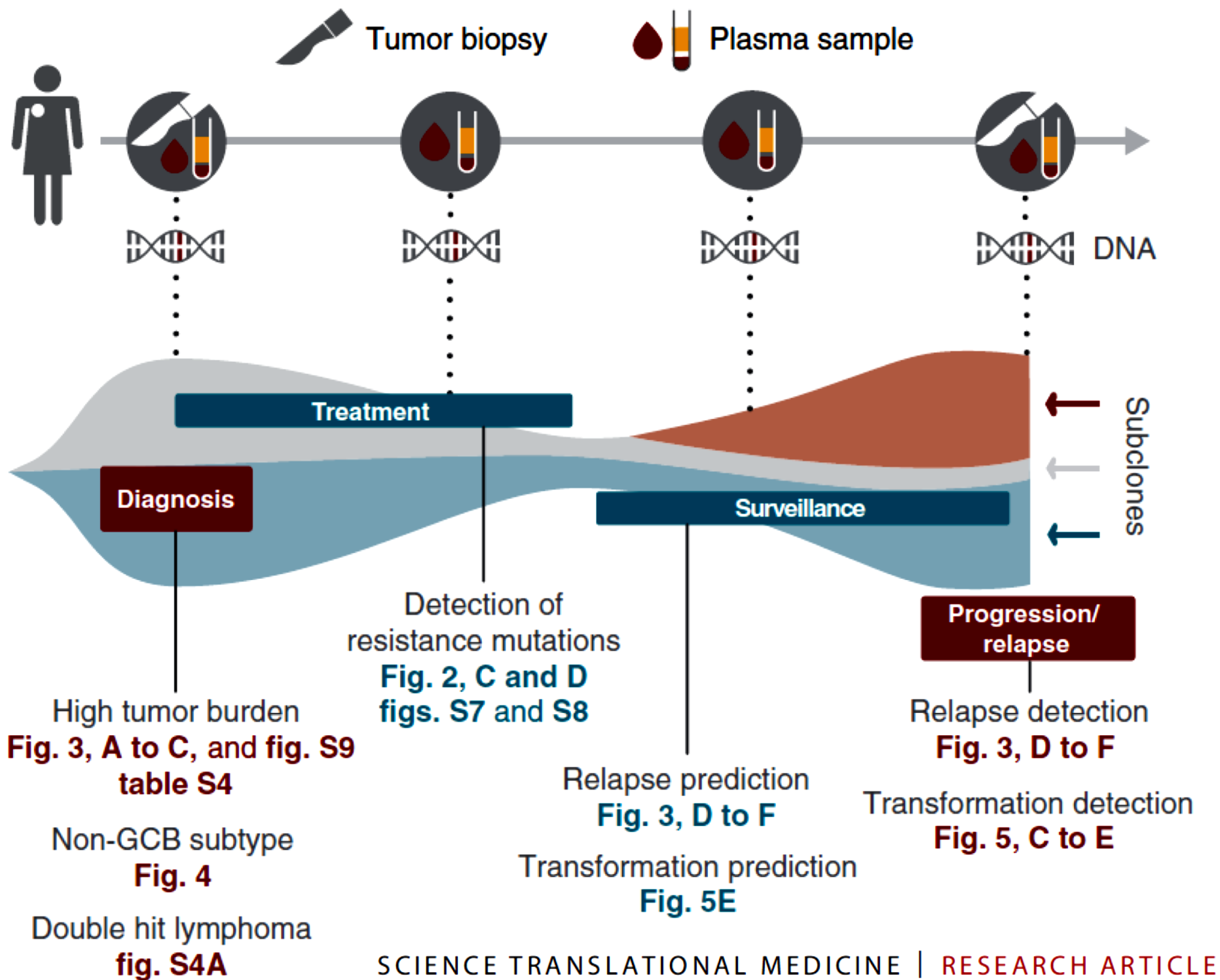
Drug treatment

Clonal selection



Drug treatment







Journal of The Ferrata Storti Foundation

Cell-free DNA sequencing as a potential screening tool for phase I targeted treatment in refractory/relapse diffuse large B cell lymphoma

by Cyril Quivoron, Anthony Tarabay, Jean-Marie Michot, Arnaud Pagès, Hélène Lecourt, Anne Aupérin, Alina Danu, Julien Lazarovici, Julien Rossignol, David Ghez, Peggy Dartigues, Véronique Vergé, Christophe Massard, Valérie Camara-Clayette, Vincent Ribrag, and Clémentine Sarkozy

Received: December 15, 2021.

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